



Ministry of Health Sri Lanka

National Guidelines

Clinical Management of Dengue Infection in Pregnancy

In collaboration with

Sri Lanka Medical Association

Sri Lanka College of Obstetricians and Gynaecologists

Ceylon College of Physicians

July 2019

Ministry of Health – Sri Lanka

Guidelines for Clinical Management of Dengue Infection in Pregnancy

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In collaboration with



SLMA



SLCOG



EPIDEMIOLOGY
UNIT



CCP

This document includes the latest concepts on management of dengue haemorrhagic fever in pregnant women. It is an extension to the existing National Guidelines on Clinical Management of DF/DHF in Adults, published by Epidemiology Unit, Ministry of Health in November 2012.

These guidelines were developed based on the best available evidence at the time of writing. It will be revised periodically when new evidence becomes available.

Please forward your comments and suggestions to the following address by post or email.

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FOREWORD

Dengue illness continues to be a major health problem in the South and South-east Asian regions and Sri Lanka is no exception. The out-patient and in-ward departments of most hospitals in Sri Lanka are seeing an increase in the number of adolescent and adult patients with dengue. In this backdrop, growing number of pregnant women infected with dengue virus can have poor outcome without early identification and proper medical care.

This new national guidelines on clinical management of dengue in pregnancy, developed by the Epidemiology Unit, Ministry of Health in collaboration with the Sri Lanka Medical Association, Sri Lanka College of Obstetricians and Gynaecologists and the Ceylon College of Physicians is expected to further improve existing knowledge and bridge any gaps on this subject. I take this opportunity to thank all experts who were involved in developing this guideline.

This authoritative document should be used in all levels of health care provision in both public and private settings in Sri Lanka for the management of dengue and dengue haemorrhagic fever patients who are pregnant. I am sure this document will help in strengthening the case management and ultimately reduce the number of severe cases and bring down the deaths due to dengue associated with pregnancy in Sri Lanka, further.

Dr. Anil Jasinghe
Director General of Health Services

PREFACE

At the induction ceremony of the President of the SLMA held in January 2019, the title of the address and the theme for the SLMA for 2019 was introduced as “Facing the challenges and forging ahead for better health outcomes”. One of the main challenges I have mentioned was reducing the morbidity and mortality from dengue in Sri Lanka. Soon after my induction, I was requested by the Director, National Dengue Control Programme, Dr. Hasitha Tissera to invite all stakeholders to form an expert committee to prepare and publish a clinical management guideline to reduce the maternal morbidity and mortality from dengue fever (DF) and dengue haemorrhagic fever (DHF).

In recent years Sri Lanka has been successful in reducing the incidence and mortality from DF/DHF. This has resulted from concerted and persistent efforts by the Epidemiology Unit and National Dengue Control Unit of the Ministry of Health. Public awareness has been increased about causation, breeding sites and early recognition of DF/DHF. Management of DF/DHF among the medical profession has improved considerably due to the nationwide dissemination of the national guidelines regarding management of dengue. This is confirmed by the table below.

Yearly dengue incidence 2016 - 2018

Year	No of Cases	Case Rate/ 100,000	No of deaths	Case fatality rate
2016	55,150	250	97	0.290%
2017	186,101	930	440	0.23%
2018	50,163	250	56	0.11%
Target (2023)	20,000	100	20	<0.1%

Source: National Dengue Control Programme, Annual Report – 2016 - 2018

Despite the overall reduction in morbidity and mortality from DF/DHF, the mortality from maternal dengue remains unacceptably high. In fact, DHF was the leading cause of maternal deaths in the analysis of maternal mortality in Sri Lanka, as indicated by the table below.

Maternal Mortality 2016 and 2017

Year	Maternal mortality/ 100,000 live births	No. of dengue deaths/ total no. of maternal deaths	Dengue rank in causes of deaths
2016	33.8	6 / 112	11 th cause
2017	39	21 / 127	1 st (Leading cause)

Source: Family Health Bureau - Annual Report – 2016 & 2017

Needless to say, the mere mention of dengue as the cause of illness results in much anxiety and stress among the relatives of the affected. The knowledge that a pregnant mother has dengue increases anxiety tremendously.

The SLMA is extremely happy to give leadership to the development of guidelines to reduce the maternal morbidity and mortality from DF/DHF. I thank all members of the expert committee who have worked diligently in the development of the guidelines. My special thanks are due to the convener, Dr. Hasitha Tissera, the driving force behind the development of this document. I sincerely hope that the guidelines will be practised by the clinicians and will assist them in ensuring safe delivery of mothers affected with dengue and the delivery of healthy babies.

Dr. Anula Wijesundere,
President, SLMA

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CHAPTER 1 : INTRODUCTION

Concern regarding women who are pregnant getting infected with dengue virus has been heightened in recent years due to an increase in adolescent and adult infections. Pregnant women with dengue need early identification. Clinical management requires a multi-disciplinary approach and precise time related interventions for optimal outcome. Early detection and access to proper medical care will reduce complications and mortality.

This guideline on clinical management of dengue in pregnancy was developed on clinical experiences, expert committee reports, publications and opinions of practising clinicians based on best available evidence at the time of writing. Further, there has been a substantial reduction in complications and unwarranted deaths in clinical settings practising the guidance given herein.

1.1 CLINICAL MANIFESTATIONS

Dengue virus infection may be asymptomatic or cause of a spectrum of symptomatic disease such as undifferentiated febrile illness, dengue fever (DF), or dengue haemorrhagic fever (DHF) including dengue shock syndrome (DSS). Out of the symptomatic dengue, DF and DHF are the two main clinical entities, collectively considered as Dengue Illness. Dengue fever (DF) and DHF are distinct from each other as DHF is characterized by a period of transient plasma leakage due to increased capillary permeability, specifically noted in the pleural and peritoneal spaces. When the leaking is massive and not compensated the resulting hypovolaemia in the vascular space will lead to shock known as dengue shock syndrome (DSS). The duration of leaking, known as the 'critical phase' is usually 24-48 hours. Occasionally it can be shorter but unlikely to go beyond 48 hours. DF is commoner than DHF, but the risk of developing DHF is higher in individuals who have developed dengue more than once. Haemorrhage, though more likely in DHF, is common to both DF and DHF.

Dengue fever (DF) is more common in older children, adolescents and adults. It is generally an acute febrile illness with severe headache, myalgia, arthralgia, rashes with leucopenia and thrombocytopenia. Although DF is usually benign, it could be incapacitating with severe headache, muscle, joint and bone pain, particularly in adults. Occasionally DF patients will have unusual

haemorrhage such as gastrointestinal bleeding, hypermenorrhoea and massive epistaxis or occult bleeding.

Traditionally, dengue haemorrhagic fever (DHF) was more common in children less than 15 years of age in association with repeated dengue infection (secondary infection) with a different virus serotype. However, the incidence of DHF in adults, including pregnant women, is increasing. Unlike in DF where usually patients will have a brief febrile phase followed by convalescent phase, in DHF, patients will have transient plasma leakage into interstitial and serosal spaces (known as Critical Phase) which has a tendency to develop hypovolemic shock (dengue shock syndrome). Preceding *warning features* such as persistent vomiting, abdominal pain, lethargy or restlessness, or irritability and oliguria are important for early detection of impending shock and intervention to prevent shock. Altered vascular permeability (**Plasma leakage**) and abnormal haemostasis (**Bleeding**) are the main pathophysiological hallmarks of DHF.

More recently, with the geographical spread of dengue illness and with more involvement of adults, there has been reports of DF and DHF with unusual or atypical manifestations. These include isolated organ involvement such as neurological, severe hepatic, renal and other organs. These could be explained as complications of profound and prolonged shock or associated with underlying co-infections or co-morbidities. Although a rare clinical entity, such manifestations are now categorized as expanded dengue syndrome (EDS). Only a rare minority of patients can be classified as EDS.

1.2 GESTATION AND DENGUE

A higher percentage of more severe form of dengue known as Dengue Haemorrhagic Fever (DHF) occurs among pregnant women compared to non-pregnant women infected with the dengue virus. The overall severity of DHF is also higher in pregnant women than non-pregnant women.

Furthermore, acute dengue illness during third trimester will increase the risk of foetal compromise due to maternal haemodynamic decompensation, inadvertently requiring higher chance of surgical interventions for delivery.

Early bleeding due to gastric erosions should be anticipated in dengue patients who have taken NSAIDs or steroids. However, even without NSAIDs or steroids, overt or occult bleeding can occur in dengue, especially in DHF. Traumatic procedures during delivery, such as instrumentation or surgery will increase the risk of bleeding. Labour during dengue illness can be associated with worse maternal outcomes as a result of massive bleeding due to surgical interventions such as caesarean section and operative vaginal delivery.

Both mother and the newborn with dengue infection, if progress to DSS undetected, may be at an increased risk of severe haemorrhage due to coagulopathy. Common causes of death in pregnant women with dengue can be due to prolonged shock with multi-organ failure, massive bleeding, fluid overload or due to a combination of the above conditions. Delayed or misdiagnosed DHF/DSS in the early stage will lead to complications and can even cause death.

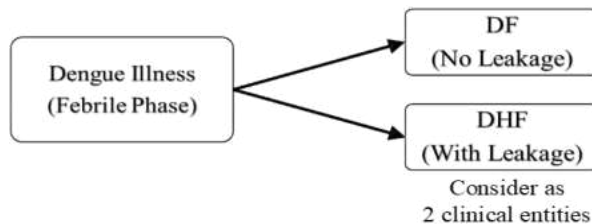
The risk of vertical transmission is well established among women with dengue during the late pregnancy period. All babies born to such mothers should be closely observed during perinatal period.

CHAPTER 2 : NATURAL COURSE OF DENGUE ILLNESS

Dengue viral infection may be asymptomatic or may cause a spectrum of symptomatic clinical disease with following possible outcomes (*Extracted from the National Guidelines*) both in pregnant and non-pregnant women.

1. Undifferentiated Fever
2. **Dengue Fever (DF)**
3. **Dengue Haemorrhagic Fever (DHF)**
4. Expanded Dengue Syndrome (EDS)

Among symptomatic dengue patients DF and DHF are the most significant two clinical entities encountered in practice. During the initial few days termed as **febrile phase** both these groups are clinically similar. While DF patients progress to convalescent phase as temperature settles, DHF patients develop the **Critical Phase** due to altered vascular permeability leading to plasma leakage. Hence, the hallmark of DHF is plasma leakage which is not seen in DF.



2.1 CLINICAL DIAGNOSIS OF DENGUE ILLNESS

Early diagnosis of Dengue illness on the first day of fever or at first contact point relies on high index of suspicion. Clinical features used in non-pregnant women can be used to diagnose probable dengue in pregnant women as well.

Dengue during pregnancy may lead to unwarranted consequences unless specific attempts are made to make an early diagnosis. Dengue should be considered high up in the differential diagnosis in any pregnant woman presenting with acute fever, from any part of Sri Lanka in the present hyper-endemic context.

2.2 DENGUE FEVER

Dengue Fever (DF) is generally an acute febrile illness (usually due to primary dengue virus infection from any of the 4 serotypes), with non-specific clinical signs and symptoms. Although DF is a benign condition, rarely can be associated with **unusual bleeding** which is a cause of death in DF, if not recognized and treated early.

- Diagnosis of DF is based on clinical, laboratory and epidemiological criteria.

Clinical and laboratory findings are as follows;

Signs and Symptoms of Clinical Dengue Fever (DF)

- Acute onset of high grade fever (Day 1 to 7) with body aches, facial flushing/ diffused blanching erythema of the skin, back pain, myalgia, arthralgia, retro orbital pain, headache, nausea, vomiting, anorexia, and diarrhoea. Some patients may have sore throat, injected pharynx, and conjunctival injection.
- Rash looks like flushed skin on day 1 to 2, which may resemble measles later or mimic as pregnancy rash.
- Fever associated with respiratory symptoms such as cough and coryza should not exclude the possibility of Dengue illness. Even if such symptoms are suggestive of Influenza, patient should be monitored with repeated FBC and treated symptomatically.
- While rapid NS1/IgM tests will provide an aetiological diagnosis, a negative result should not exclude dengue if clinically suggestive.
- Minor bleeding can manifest as petechial haemorrhages, mucosal bleeding or epistaxis. However, bleeding may be heavy in some patients if they are on medications such as Aspirin, NSAIDs, steroids or long-term anti-platelet drugs.
- Occasionally, unusual haemorrhage such as gastrointestinal bleeding, hypermenorrhea and massive epistaxis may occur, especially GI bleeding is seen in those having an underlying peptic ulcer disease.
- Physical examination may reveal no focus of infection except facial and skin flushing with posterior cervical lymphadenopathy.

Dengue viraemia in a patient is short, typically occurring a day or two before the onset of fever and lasts for up to four to seven days of illness. During this period the dengue virus, its nucleic acid and

circulating viral antigen can be detected. Viral antigen detection (NS1) has become the most common early diagnostic tool, due to commercially available rapid test kits.

NS1 Antigen and IgM/IgG Antibodies – results depend on the tested day of fever; NS1 usually diagnostic on first 3-4 days. Anti-dengue IgM antibody is usually detectable by day 5 of the illness or later, i.e. only NS1 is positive during first few days of illness. In most patients IgM may persist up to 60 days. In primary infection IgG is usually detectable little after IgM and in secondary infection IgG will become positive early. Therefore, IgG might be useful to differentiate primary and secondary dengue infections. If IgG is positive by day 3 it would indicate a secondary infection and may have some use in predicting DHF. However, results could also depend on the sensitivity and specificity of the commercially available test kits. If clinically suggestive of dengue, even if NS1 is negative, consider dengue as a possibility and manage accordingly.

In specialized laboratories with molecular biology facilities *RT-PCR* remains the gold standard of aetiological confirmation. The advantage of this test is its high sensitivity and specificity on acute sample and identification of serotypes. It is, however, an expensive technology that requires sophisticated instruments and skilled professionals.

Full Blood Count (FBC) -

- Fever/history of fever and other clinical features with leukopenia (WBC <5,000 cells/ μ l), is strongly suggestive of dengue in endemic areas. However, in pregnancy, leukopenia may not be a feature (often WBC could be normal or high) and serial FBC may only show a drop in the total WBC count with a significant reversal of lymphocyte to neutrophil ratio with atypical cells in the blood picture.
- Progressive decrease in WBC count is an early indication of dengue.
- Thrombocytopenia (<150x10⁹/L)
- Hematocrit (HCT) could be normal or high

UFR – presence of few pus cells and red cells should not exclude dengue (even if UTI is suspected).

Epidemiologically, dengue is endemic (constantly reported year round) in many parts of Sri Lanka. In such endemic areas dengue transmission occurs in clusters (several patients reported from one

locality in a particular time period). Therefore, the treating clinician should ask for history of diagnosed cases of dengue in the family or immediate neighborhood during the past two weeks when a febrile patient presents to the consultation (spacio-temporal clustering). However, practitioners in non-endemic areas are likely to receive isolated patients who have acquired dengue infection from endemic areas (due to travel), particularly during outbreak seasons.

Presence of fever with at least 2 signs and symptoms mentioned above with thrombocytopenia are sufficient to suspect dengue illness (fever +2+1) in pregnancy.

2.3 DENGUE HAEMORRHAGIC FEVER (DHF)

In the first few days of DHF, patients will have signs and symptoms similar to DF. However, in DHF, (usually beyond day 2) patient will develop features of **plasma leakage** and **bleeding** which are the hallmarks of DHF. Abnormal haemostasis in DHF can cause concealed or overt bleeding which may be significant in some patients.

Features of DHF includes:

1. Fever: acute onset high fever or recent history of acute fever
2. Haemorrhagic manifestations* (at least in the form of a positive tourniquet test)
3. Thrombocytopenia of $<130 \times 10^9/L$ with a rising HCT (towards 20%)
4. Objective evidence of selective capillary plasma leaking into chest and abdominal cavities (visualization of fluid in the peritoneal cavity and pleural space by real-time ultra sound scan of the abdomen and chest).

**In patients who have evidence of plasma leakage, presence of haemorrhagic manifestations is not essential for the diagnosis of DHF. However, DHF patients may develop overt or concealed bleeding during the course of the illness.*

Onset of leaking is usually heralded by:

- Settling of fever (defervescence)
- FBC changes
 - WBC tends to rise following a progressive fall to a nadir (lowest value)
 - Thrombocytopenia ($<130 \times 10^9/L$)
 - Hematocrit (HCT) rising above the baseline

2.3.1 NATURAL CAUSE OF DHF

Unlike DF, which has a febrile phase followed by a convalescent phase, DHF patients have 3 phases which include a critical (leaking) phase between the febrile and convalescent phases. Therefore, DHF patients are different from DF patients in that they have **plasma leakage** during the critical phase.

- 1) Febrile Phase (similar to that of DF - Refer Section 2.2)
- 2) Critical Phase (Section 2.3.2)
- 3) Convalescent Phase (Refer Chapter 8)

DHF has two clinical entities: (1) DHF without shock and (2) DHF with shock (Dengue Shock Syndrome - DSS). Therefore, in any pregnant woman who presents with shock (particularly afebrile at presentation) consider DSS as a likely diagnosis.

2.3.2 CRITICAL PHASE IN DHF

Critical phase occurs towards the late febrile phase, often after the end of 2nd day of fever, usually around the 4th or 5th day of illness with defervescence (settling of fever). Some patients may enter the critical phase while having high fever. However, in pregnancy this may occur outside the usual duration, earlier or later. Therefore, daily Full Blood Count (FBC) assessments together with regular and frequent HCT and ultrasound scans of abdomen and pelvis of pregnant dengue patients are important to identify plasma leakage as early as possible.

Dengue fever with haemorrhagic manifestations must be differentiated from dengue haemorrhagic fever heralded by plasma leakage.

in DF – no plasma leakage

in DHF – plasma leakage is seen

Settling of fever is NOT ALWAYS a sign of recovery, as the patient may leak when fever settles.

Plasma leakage in DHF is selective, transient and self-limiting, usually lasting 24-48 hours.

2.3.3 WARNING FEATURES OF SIGNIFICANT CAPILLARY PLASMA LEAKAGE IN DHF

Patients should be closely observed for following features predicting significant plasma leak. If not detected and treated appropriately it can lead to hypovolemic shock and complications. However, some DHF patients may develop shock due to significant plasma leakage without any warning features.

- Clinical deterioration with settling of fever
- Severe abdominal pain
- Excessive vomiting
- Bleeding (epistaxis, gum bleeding, melaena, vaginal bleeding)
- Impaired consciousness or behaviour changes
- Cold-clammy peripheries
- Prolonged Capillary Refill Time (CRFT >2 seconds)
- No urine output for 4-6 hours

2.3.4 FEATURES OF FLUID LEAKAGE

Features suggestive of fluid leakage:

- Narrowing of pulse pressure with increasing diastolic pressure, tachycardia with low-volume pulse ($>100/\text{bpm}$), tender hepatomegaly and reduced urine output.
- Haematocrit (HCT) rise (increase of 10% –15% above baseline is an early indirect evidence of plasma leakage); check for rising trend of HCT from baseline value obtained from FBC done on first few days of febrile phase or normal ANC follow up value. If no baseline hematocrit is available consider HCT 32 - 34% as the baseline.
- Platelet counts less than $130 \times 10^9/\text{L}$ or a rapid drop in platelet count (e.g. Platelet count of $200 \times 10^9/\text{L}$ falls to $80 \times 10^9/\text{L}$ same day).
- Prolonged CRFT and postural hypotension.

Biochemical investigations such as serum albumin and non-fasting cholesterol are not useful during pregnancy.

Features confirming fluid leakage:

- Selective ultrasonography (USS) of chest and abdomen for evidence of plasma leakage into the third space. There can be a time gap from initial point of leaking to USS detection of fluid in pleural and peritoneal cavities. During this period the hematocrit and heart rate may go up or else, the UOP may drop, suggesting leaking. In such patients, **repeat interval USS** to see whether there is objective evidence of leaking. Eventually, in all DHF patients with significant plasma leakage, fluid will be detectable by USS. If repeated USS does not show fluid and if the patient is haemodynamically unstable, reduced UOP and low PCV, consider alternative diagnosis (bleeding).
- Clinical accumulation of fluid in peritoneal and pleural spaces (late finding).

Do not depend exclusively on USS for diagnosis of leakage. Other parameters such as settling of fever, vital signs, platelet count, gradual rise in HCT and reduced urine output are important to diagnose the onset of leaking in DHF. However, demonstration of fluid in the peritoneal cavity and pleural space on repeated ultrasound scan confirms that the patient has developed leakage of plasma and is progressing **(patient in critical phase of DHF)**.

2.3.5 ULTRASOUND FEATURES OF PLASMA LEAKAGE IN DHF

- Bedside ultrasound scan of the abdomen and the chest on supine position, with no preparation, identify fluid in body spaces and cavities.
- Presence of oedema of the gall bladder wall with no fluid around it, is not a feature of plasma leakage. However, this generally precedes plasma leakage. Therefore, it warrants a repeat scan in 4-6 hours to identify possible plasma leakage.
- Gall bladder wall oedema with a thin rim of fluid around it, is the earliest sonographic finding in plasma leakage.
- Thin rim of fluid in hepato renal recess, indicates approximately six hours has elapsed since beginning of plasma leakage.
- Fluid in the peritoneal cavity, among bowel loops and in the pelvis, indicates more than six hours have elapsed since beginning of plasma leakage.
- Fluid in the pleural space, is commonly seen on the right side and indicates more than six hours have elapsed since beginning of plasma leakage.
- Fluid in the perirenal space, is commonly seen on the right side. This indicates more than six hours have elapsed since beginning of plasma leakage.
- In a patient where bi-lateral pleural effusions and ascites is seen; implies that the patient is in the latter part of the critical phase when major portion of leaking (probably >50% of leaking) is over. Fluid therapy for such patients should be carefully guided (vital signs and HCT) as increased rates of fluid can lead to fluid overload.

2.4 DENGUE SHOCK SYNDROME (DSS)

DSS will have, DHF criteria mentioned above and evidence of circulatory failure (hypovolemic shock) in pregnant women observed with;

- **Clinical signs of shock:** rapid and weak pulse with delayed CRFT, cold-clammy skin or skin mottling;
- **Narrowing of pulse pressure** to 25mmHg (compensated shock due to **plasma leakage**);
- **Rising HCT** $\geq 30\%$ from baseline and thrombocytopenia;
- **Hypotension** (sBP < 80 mmHg) with postural giddiness - if present consider possibility of **bleeding** in addition to leaking (decompensated shock probably due to leaking and bleeding).

Pathophysiology of shock in DSS is usually due to **plasma leakage** and subsequent **heavy bleeding** when leaking is not corrected. But, presence of hypoglycemia, excessive vomiting leading to dehydration and sepsis due to co-infection may also contribute towards a state of shock.

Chapter 3 : PHYSIOLOGICAL CHANGES IN PREGNANCY AND ITS RELATIONSHIP TO DENGUE

Significant physiological changes take place in all organ systems during pregnancy, labour and in the postpartum period. Thorough understanding of these changes and application of that knowledge into practice is important in the management of a pregnant dengue patient.

3.1 CARDIOVASCULAR CHANGES

3.1.1 PULSE RATE

Heart rate, which rises throughout gestation, peaks in the late third trimester. The upper limit of resting heart rate is typically not greater than 95 bpm.

Implications on management of Dengue in pregnancy - Pregnant women with resting heart rates >100 bpm (without fever) are generally considered to have tachycardia and warrant further evaluation.

3.1.2 SYSTEMIC VASCULAR RESISTANCE AND BLOOD PRESSURE

Systemic vascular resistance progressively drops by approximately 35 to 40 percent in the mid-second trimester. Reduced SVR leads to low DBP

DBP and mean arterial pressure decrease more than SBP during pregnancy. This will lead to increase in pulse pressure. Arterial pressures begin to increase during the third trimester and return close to preconception levels postpartum.

Implications on management of Dengue in pregnancy – The change in blood pressure will lead to wider pulse pressure in pregnancy. Narrowed pulse pressure of ≤ 25 mmHg indicates **compensatory shock** in dengue with pregnancy. Pulse pressure dropping from 30mmHg to 25mmHg is strongly suggestive of patient heading towards compensatory shock requiring immediate attention.

Impact of maternal posture on Blood Pressure – The degree of change in BP is acutely influenced by posture. Assumption of the supine position can lower the venous return to the heart by 30-40% due to compression of the inferior vena cava by the gravid uterus, leading to a substantial reduction in cardiac output, hence the blood pressure. Maternal hypotension and compression of aorta by gravid uterus lead to reduction of the utero-placental blood flow.

Implication in the management of Dengue in pregnancy – Always measure the blood pressure in the complete left lateral or 15-30 degree left laterally tilted position. In order to minimize ineffective resuscitation of pregnant women with dengue, acquiring this position is crucial.

SUPINE HYPOTENSIVE SYNDROME IN PREGNANCY

Gravid uterus compresses both IVC and aorta in supine position. Pregnancy results in development of hypotension, tachycardia (occasionally bradycardia) and syncope called supine hypotensive syndrome. The normal blood pressure is quickly restored by turning the patient to left lateral position.

In a DHF patient with plasma leakage, postural hypotension is a feature of volume depletion (due to leaking/bleeding or both) which may be misinterpreted as supine hypotension syndrome (and vice versa).

3.1.3 PULMONARY VASCULAR RESISTANCE

There is a reduction in pulmonary vascular resistance, increased pulmonary blood flow with normal mean pulmonary artery pressure. Serum colloid osmotic pressure is reduced by 10–20% due to reduced albumin level. The colloid osmotic pressure/pulmonary capillary wedge pressure gradient is reduced by about 30%, making pregnant women particularly susceptible to pulmonary oedema. Pulmonary oedema will be precipitated if there is either a sudden increase in cardiac pre-load (such as rapid fluid bolus) or increased pulmonary capillary permeability (such as in pre-eclampsia) or both.

Implications in the Management of Dengue in pregnancy – Any leaky capillary state may easily precipitate pulmonary oedema e.g.: excessive use of IVF. As Dengue Haemorrhagic Fever (DHF) is also a leaky capillary condition, a pre-eclamptic woman with Dengue may have a high-risk of developing severe pulmonary oedema

3.1.4 PLASMA AND BLOOD VOLUME

Plasma volume expands progressively until 30 to 34 weeks, and then plateaus or decreases slightly through term. The total gain at term is 30 to 50 percent above that in non-pregnant women.

Blood volume gradually increases and reaches about 50% by the 30th week of POA, with a similar increase in venous return and cardiac output until term. Further increases take place during labour due to uterine contractions and sympathetic stimulation due to pain. Soon after delivery, **release of aortocaval compression with complete uterine retraction divert about 400-500 ml blood in to circulation, known as autotransfusion.**

Implications on Management of Dengue in pregnancy – Generally it is not recommended to transfuse blood after delivery if the blood loss is normal. A pregnant woman with dengue may not show features of hypovolemia even with significant blood loss until late stages (hypotension will appear later than in a non-pregnant woman). Therefore, a blood transfusion is recommended in DHF even with a normal blood loss (<500 ml).

Utero-placental blood flow has no autoregulation and is dependent on maternal mean arterial blood pressure for its blood flow. Any reduction in maternal blood pressure can negatively impact the uterine blood flow and consequently reduce the utero-placental flow, thereby compromising foetal perfusion and oxygenation. Uterine vasculature is exquisitely sensitive to catecholamines and that too can lead to reduction in utero-placental blood flow. In fact, **foetal distress** may be the first indication of **maternal hemodynamic decompensation** in pregnancy with leaking in dengue.

3.2 HAEMATOLOGICAL AND BIOCHEMICAL CHANGES IN PREGNANCY BY TRIMESTER

3.2.1 INCREASED RED CELL MASS

Red blood cell (RBC) mass steadily rises, up to levels 20 to 30 percent higher by the end of pregnancy. However, the increase in RBC mass is smaller than the increase in plasma volume, which contributes to the physiologic anemia of pregnancy. Normal Hb is 10.5 - 13.5g/dl and haematocrit is 32-34%.

Implications in the Management of Dengue in pregnancy - HCT of 38-40% may indicate leaking in DHF (HCT rising towards 20%).

3.2.2 WHITE CELL COUNT AND IMMUNITY

Pregnancy is associated with leukocytosis. WBC counts range from 9000 to 15,000 cells/ μ l, while further rise may occur during labour up to 25000/ μ l.

Cell mediated immunity is suppressed to prevent rejection of foetus, making pregnant women more susceptible to viral infections such as Dengue.

Implications in the Management of Dengue in pregnancy – WBC < 5000cells/ μ l. (leucopenia) may not be seen in febrile phase. A downward trend of WBC is important even in the absence of leucopenia.

3.2.3 PLATELET COUNT

A mild decrease in the platelet count, from pre pregnant levels, occurs in all women during an uncomplicated pregnancy. Gestational thrombocytopenia (GT) is the commonest cause of isolated thrombocytopenia in pregnancy. However, GT occurs during the second and more commonly in third trimester. The platelet count seldom drops to <80x10⁹/L in GT. The commonest cause of thrombocytopenia in the first trimester is immune thrombocytopenia. All women with a platelet count <100x10⁹/L should be investigated to ascertain its aetiology.

Implications in the Management of Dengue in pregnancy – In a patient with fever/history of fever and a low platelet count it is mandatory to exclude Dengue illness. It is also important to look at changes in repeat platelet counts and study the trend.

In pre-eclampsia and HELLP syndrome thrombocytopenia is a common feature. Therefore, it is necessary to exclude dengue before intervention.

If platelet count is $<50 \times 10^9/L$ spinal anesthesia is contraindicated. Epidural labour analgesia or anaesthesia is contraindicated when platelet count is $<80 \times 10^9/L$. This is to prevent spinal haematoma formation and resultant spinal cord compression. However, if coagulation is not deranged, an experienced Anaesthetist may consider a careful single-shot spinal for caesarean section, after platelet transfusion to increase platelet count to $>50 \times 10^9/L$, in special situations such as predicted difficult airway. General anesthesia is advisable.

For Caesarean section platelet transfusion is required when the count is $<50 \times 10^9/L$ and for vaginal delivery platelet transfusion is required when the count is $<30 \times 10^9/L$. Caution should be exercised to avoid fluid overload in DHF and therefore, platelet concentrate might be a better option.

3.2.4 COAGULATION IN PREGNANCY

Normal pregnancy is a prothrombotic state. Compared with non-pregnant women, pregnant women have a marked increase in some coagulation factors, reduced fibrinolysis, and increased platelet reactivity. As a consequence, there is increased risk for thromboembolic complications.

The activated partial thromboplastin time (APTT) and the prothrombin time are slightly decreased (shortened). INR is usually < 1 .

Fibrinogen levels in normal pregnancy is 3-5g/L, which is much higher than in non-pregnant women; levels in the third trimester is higher, ranging from 3.7 to 6.2 g/L.

Implications in Management of Dengue in pregnancy - Reduced platelet increases risk of bleeding with unstable clot. Consumptive coagulopathy can be developed easily, especially in the presence of a placental abruption.

Thromboelastometric (ROTEM) evaluation of coagulation is useful to detect, correct and re-evaluate any derangement, (using validated dose calculation charts and algorithms), before vaginal delivery, caesarean section and in patients with heavy bleeding after delivery. The main advantages include targeted, **early correction without overloading** the patient by replacing only the required factors including platelets in smaller volumes and avoidance of unnecessary factor transfusions.

3.2.5 SERUM ALBUMIN AND NON-FASTING CHOLESTEROL LEVELS

Serum albumin is low in pregnancy, ranging from 25-28 g/L.

Implications in Management of Dengue in pregnancy - with plasma leakage in DHF serum albumin also leaks into potential spaces only to return with reabsorption. Indirect feature of reabsorption is an elevation in serum albumin level in a patient who has completed critical phase.

Non-fasting cholesterol is high in pregnancy (>40 % increase). Therefore, this is not a good indicator to identify leaking.

3.3 RESPIRATORY CHANGES IN PREGNANCY

The normal changes during pregnancy result in a compensated respiratory alkalosis, with a higher PO₂ and a lower PCO₂ than in the non-pregnant state.

Decreased FRC and stable FEV1 – Functional residual capacity (FRC) decreases approximately 20 percent during the latter half of pregnancy, making them to have less oxygen reserves than in non-pregnant state.

Increased ventilation and respiratory drive – The most striking change in respiratory physiology during pregnancy is an increase in resting minute ventilation, which rises by nearly 50 percent at term. This is primarily due to a larger tidal volume (increased up to 40 percent), whereas the respiratory rate remains essentially unchanged.

Oxygen consumption is elevated by 25-30%. Therefore, a pregnant woman desaturates faster and becomes hypoxic easily compared to non-pregnant

Implications on Management of Dengue in pregnancy – Respiratory Rate >25 breaths/min with or without dyspnoea is abnormal and may need attention. Respiratory rate is said to be the first to change as the woman becomes progressively ill (consider Acidosis/Fluid overload/impending shock).

Respiratory alkalosis - Arterial PCO₂ falls to a plateau of 27 to 32 mmHg during pregnancy. Arterial pH is normal to slightly alkalotic (usually between 7.40 to 7.45).

Implications on Management of Dengue in pregnancy - In a non-pregnant complicated dengue patient, when pH is ≤ 7.35 together with HCO₃ level <15mmol/l early correction is recommended to prevent bleeding and DIC. But in a complicated pregnant dengue patient, threshold for correction of acidosis should be early, if acidosis is persistent even after fluid resuscitation. If the patient has persistent acidosis, pH <7.35 with HCO₃ <15mmol/l it denotes **prolonged shock** and such patients are likely to have organ involvement (possible liver, kidney injury).

Maternal arterial oxygen tension - ranges from 106 to 108 mmHg. Arterial oxygen tension is higher. PaO₂ of >70 mmHg and SpO₂ of >95% needed for adequate foetal oxygen delivery.

Implications on Management of Dengue in pregnancy - In DSS (DHF with shock and/or massive fluid overload) arterial oxygen tension and SpO₂ are low due to ventilation perfusion mismatch as a result of pleural effusion. This may require mask oxygen, positive end expiratory pressure (PEEP) or mechanical ventilatory support to keep oxygen saturation >95%, and arterial oxygen tension > 70 mmHg.

3.4 RENAL CHANGES IN PREGNANCY

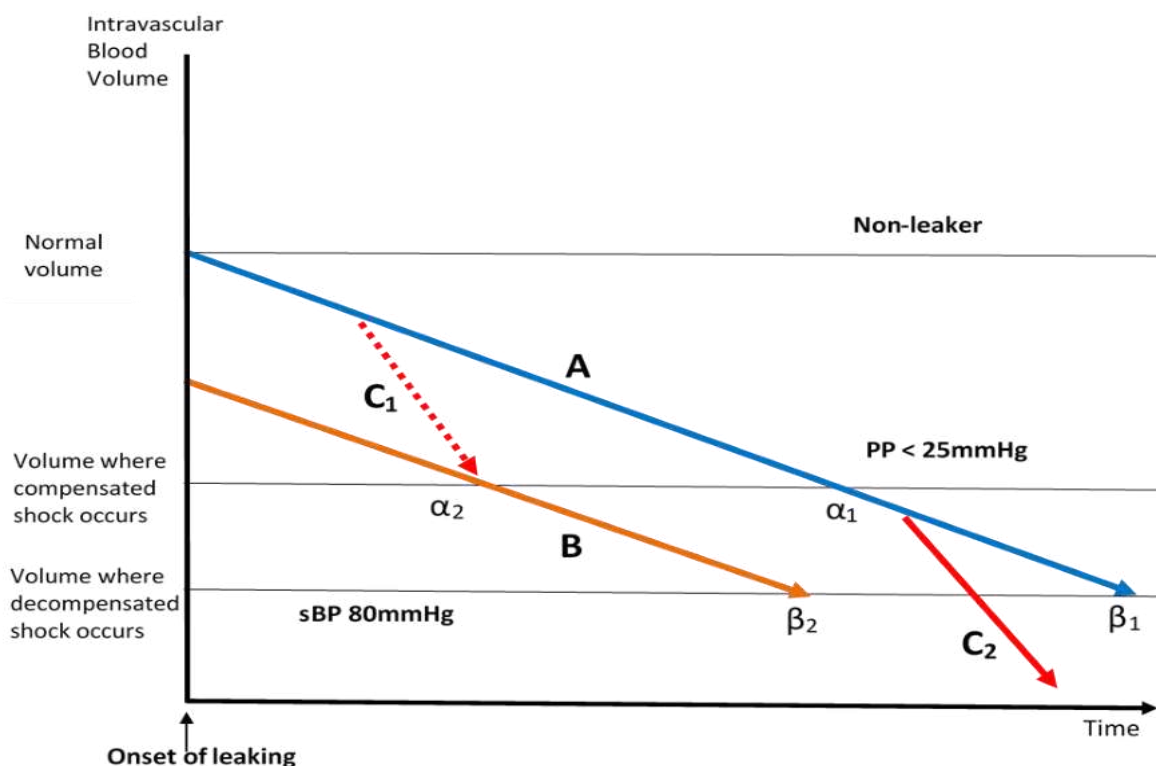
Glomerular Filtration Rate (GFR) increases by as much as 50-85%. Renal Plasma Flow (RPF) increases up to 80% as compared with non-pregnant levels. Although frequent urination is often reported in pregnant women, rarely there could be true polyuria (>3 L/day).

Implications on management of Dengue in pregnancy – In DSS (DHF with shock) with pregnancy, intense thirst may not appear and despite intravascular volume depletion a normal urine output may persist. Therefore, urine output may not be a good marker of degree of shock in pregnancy.

CHAPTER 4 : HAEMODYNAMIC CHANGES IN DENGUE SHOCK IN PREGNANCY

Pregnant woman with DHF in shock is known as Dengue Shock Syndrome (DSS). Any pregnant woman presenting in shock, DSS should be considered early, in the present hyper-endemic context in Sri Lanka. DSS is an extension of DHF state where, excessive plasma leakage has resulted in hypovolemic shock. However, in a pregnant woman with DSS, severe haemorrhage should be diagnosed early in addition to plasma leakage. Unless identified early and treated appropriately, this is a life-threatening condition.

4.1 NATURAL COURSE OF PLASMA LEAKAGE (AND ACUTE BLEEDING) IN DHF/DSS



X-axis shows time and Y-axis shows the intra-vascular blood volume in a DHF patient. This illustration of Lines A&B, are shown as linear for explanatory purposes, but in reality are curved (concave up).

Line A

- Shows leaking in a person with normal intravascular volume from onset.
- As the leakage progresses compensatory mechanisms set in resulting in progressive rise of diastolic blood pressure due to peripheral vasoconstriction, narrowing the pulse pressure and rise of heart rate. This may require increment of fluid infusion.
- The point at which the intravascular volume where pulse pressure of 25mmHg (α_1 point) should be avoided. However, if it occurs fluid has to be replaced soon (i.e. 500ml of NS within 1 hour as bolus). This α_1 point is called **compensated shock**.
- As leakage progresses the compensatory mechanisms breakdown resulting in lower sBP and the arbitrary point here is set at 80mmHg. This point β_1 is called **decompensated shock**. In DSS as viscosity of blood is increased due to leaking, organ perfusion may get compromised earlier than any other condition with low sBP. The fluid replacement here has to be rapid i.e. pushing the bolus of 500 ml as fast as possible (free flow).

Line B

- Shows leaking in a person who is already in intra-vascular volume depletion from the onset as a result of dehydration.
- This explains how a person with initial dehydration reaches critical intravascular volume earlier - α_2 . If continues to leak without treatment this patient will reach decompensated shock much earlier – β_2 point. This can also be seen in a late presenter who has already progressive leaking.

Line C (dotted and straight)

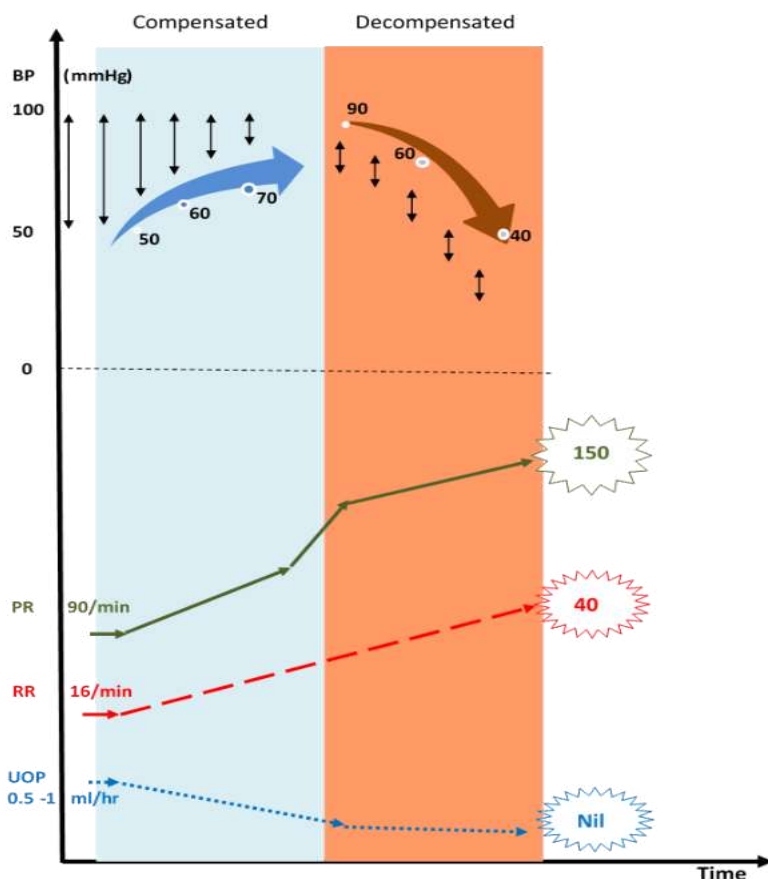
- C1: Shows a sudden bleed, which brings the intravascular volume to critical state simultaneously (α_2) with steady leakage. Commonly caused by NSAIDs and steroids with peptic ulcers or underlying bleeding tendency.
- C2: This bleed is more pronounced in later stages of DHF (prolonged and profound shock) with DIC and associated coagulopathy. Usually results from delayed admission or late recognition of DSS.

The compensatory mechanisms such as progressive rise of heart rate and reduced urine output while on fluid therapy indicate that the volume replacement is inadequate and need to increase rate of fluid replacement.

However, along with tachycardia and poor urine output if pulse pressure is narrowed $\leq 25\text{mmHg}$ (compensatory shock) or systolic BP is less than 80mmHg (decompensatory shock) resuscitate the patient with fluid bolus.

Sudden rise of heart rate (without fever or disproportional to fever) may be an indicator of bleeding. This should be confirmed with a HCT which may be low or equivocal.

4.2 CHANGES IN VITAL SIGNS AND URINE OUTPUT IN COMPENSATED AND DECOMPENSATED SHOCK



In this diagram, changes in sBP, dBP and PP are depicted above the dotted line.

Pulse rate, respiratory rate and urine output variations in the compensated and decompensated shock states are depicted below the dotted line.

Temperature during this period is usually normal (afebrile).

4.3 FEATURES OF DENGUE SHOCK IN PREGNANCY

4.3.1 COMPENSATED SHOCK

- **Main feature** - Narrow pulse pressure ≤ 25 mmHg in left lateral position.
- **Associated features** (all these may not be present at a given time):
 - Cold extremities and prolonged capillary refill time (CRFT) more than 2 seconds
 - Tachycardia (>100 bpm) with low volume pulse without fever
 - Normal sBP with raised dBP in left lateral or seated position
 - Postural hypotension
 - Intense thirst with reduced urine output or without reduced UOP in pregnancy.

Despite state of shock these patients can be fully conscious and rational.

4.3.2 DECOMPENSATED SHOCK

- **Main features**
 - sBP <80 mmHg and/or reduction in sBP by >20 mmHg
 - Mean arterial BP <70 mmHg or unrecordable BP at left lateral position
- **Associated features** (all these may not be present at a given time):
 - Change of mental state e.g.: restless, combative or lethargy
 - Prolonged CRFT with mottled skin, cold-clammy extremities
 - Severe tachycardia with weak or absent peripheral pulses
 - Oliguria or anuria
 - Tachypnea with metabolic acidosis.

In pregnant women with decompensated shock early assessment of degree of shock is important. Such patients can be further classified as:

- a) **Prolonged shock** – shock lasting more than 4 hours. No passage of urine for 4-6 hours is a predictor to be confirmed by urinary catheterization (catheter to be inserted carefully as trauma during procedure can cause bleeding).
- b) **Prolonged and profound shock** – when the patient presents with no peripheral pulses and BP unrecordable. This condition is complicated with - Acidosis, Bleeding, Hypocalcaemia/hyponatraemia and hypoglycaemia (A, B, C, S)

CHAPTER 5 : MANAGEMENT OF DENGUE IN PREGNANCY

5.1 EARLY MANAGEMENT AND ADMISSION/REFERRAL

5.1.1 FIRST CONTACT CARE LEVEL/OPD

- Recognize:
 - pregnancy and its trimester
 - Suspect dengue early in a patient presenting with acute febrile illness.
 - Look for progressive decrease in WBC count and thrombocytopenia in fresh FBC.
 - May screen with RDT-NS1 (within 4 days) or IgM/IgG in late presenters (more than 4 days).
 - Even if NS1 is negative if the clinical features and FBC are suggestive of dengue, the patient should be managed as dengue.
 - Differentiate DHF from DF. Perform ultrasound scan of abdomen and chest to identify fluid in body cavities and spaces and monitor haematocrit (PCV).

- React:
 - In the 1st and 2nd trimesters if the patient is haemodynamically stable, admit to ward. If haemodynamically unstable admit to ETU/HDU.
 - In the 3rd trimester of pregnancy (not in labour) the patient needs early attention through multidisciplinary team (MDT), and inward care for assessment and close monitoring by Obstetric and Medical teams.
 - Women in labour or in late third trimester should be immediately reviewed by MDT for further course of action.

- Reduce:
 - Reduce late admission to hospital with complications.
 - Prevent fatalities through early referral to receive appropriate DHF management.

5.1.2 ADMISSION CRITERIA

- All pregnant women with acute onset of fever should be advised to get admitted early to a hospital, where specialist cover is available (despite normal FBC) for further care. First contact doctor should make a comprehensive assessment of the patient in order to decide on resuscitation at ETU or management at Obstetric/Medical Unit, irrespective of the duration of fever.
- Area Medical officer of Health (MOH) should encourage Field Health Staff, particularly Family Health Officer (PHM) and Public Health Inspector (PHI) to identify and refer all pregnant women with fever seen in the field to local hospital.
- Admission referral letter should include the necessary details and vital parameters.

5.2 IN-WARD MANAGEMENT OF DENGUE IN PREGNANCY

Management of Dengue in pregnancy should be of multi-disciplinary approach involving Obstetric team, Physician and Neonatologist/Paediatrician.

In addition to the obstetric management aspects, special attention should be given to the following:

- a. Identify dengue illness early
- b. Differentiate DHF from DF at the early stages (Inward bed side ultrasound scan of the abdomen and chest to identify fluid in body cavities and spaces).
- c. Manage DF patients with the assistance of the medical team
- d. Identify early and refer DHF patients to the medical team
- e. Inform and update patient's family regularly and to discuss any interventions in advance (counselling).

5.3 MANAGEMENT ACCORDING TO TRIMESTER BY WHOM AND WHERE?

All pregnant patients with fever irrespective of the trimester, should be first admitted to the Obstetric ward where initial assessment and management plans are to be decided. Further management should be done in consultation with the medical team.

Suggested place of management is as follows, to be decided with the consensus of Medical and Obstetric team;

Clinical Status		1 st Trimester	2 nd Trimester	3 rd Trimester (not in labour)
DF in uncomplicated and complicated pregnancy	Whom	Obstetric and Medical team	Obstetric and Medical team	Obstetric and Medical Team
	Where	Obstetric Ward	Obstetric Ward	Obstetric Ward
DHF in uncomplicated pregnancy	Whom	Medical and Obstetric Team	Medical and Obstetric Team	Medical and Obstetric Team
	Where	Medical Ward HDU	Medical Ward HDU	HDU MICU
DSS or DHF in complicated pregnancy (e.g. GDM, PIH, pre-eclampsia, HELLP, placenta-previa)	Whom	Multi-disciplinary Team	Multi-disciplinary Team	Multi-disciplinary Team
	Where	MICU or refer to Tertiary Care Center	MICU or refer to Tertiary Care Center	MICU or refer to Tertiary Care Center

Pregnant fever patients presenting in shock should be resuscitated in ETU and admitted to HDU/MICU for further management with the involvement of multi-disciplinary team.

5.4 ASSESSMENT OF PATIENT ONCE ADMITTED TO RELEVANT UNIT

- A. Obstetric assessment should be done daily or more often depending on the trimester
- B. Medical assessment should include;
 1. Febrile phase monitoring (patient not leaking yet – Ref. 5.4.1)
 2. Critical phase monitoring in a patient with plasma leakage (Ref. 5.4.2)
- C. Investigations;
 1. Serial Full Blood Counts
 2. Radiological assessment - bedside ultrasound scan of the abdomen and chest on admission and thereafter daily or more frequently to detect plasma leakage as early as possible.

5.4.1 FEBRILE PHASE MONITORING

All pregnant women are at high-risk of severe disease and complications. Therefore, should be closely monitored until full recovery.

- Once admitted all pregnant women with dengue should be closely monitored in order to identify leaking and/or bleeding irrespective of platelet count.
- Monitoring to be done by trained nursing officer(s).
- Monitoring of temperature, BP, pulse pressure and CRFT should be **done 3 hourly** using the standard Febrile Phase Monitoring Chart (*see Annexure 1*).
- Chart urine output 4 hourly (minimum 150ml every 4 hours if pre pregnant body weight is 50kg or more) and maintain input output chart.
- Essentially monitor inward PCV 6 hourly. Direct venous PCV (measured by Micro-haematocrit machine) is a better assessment of peripheral perfusion than laboratory HCT (obtained through Haematology Analyzer).
- Daily FBC and other investigations as necessary (e.g. LFT).
- Notify on-call doctor if any high-risk features are noticed (warning signs, derangement of vital signs reduced UOP and rising haematocrit).

5.4.2 LEAKING PHASE (CRITICAL PHASE) MONITORING

- The critical (plasma leakage) period of DHF typically starts around the time of the transition from febrile to afebrile stage.
- When leaking has started, more intense monitoring of parameters on hourly basis is necessary.
- In a pregnant women with dengue illness when the platelet count drops $\leq 130 \times 10^9/L$ anticipate leaking shortly. In such patients performing HCT/PCV 3 hourly is likely to show a rising trend.
- Establish two IV accesses using large bore (preferably 18 G) IV cannulae.

Following parameters are to be monitored during the critical phase of DHF in the HDU using the Critical Phase Monitoring Chart (*see Annexure 2*)

Monitoring Parameters	Frequency
General well-being: <ul style="list-style-type: none"> • Appetite, vomiting, bleeding, giddiness, intense thirst, restlessness, clouding of consciousness. 	<ul style="list-style-type: none"> • At least twice-daily
Vital signs: <ul style="list-style-type: none"> • Temperature, PR, BP, PP and RR (by Multi-para monitor) • Pulse volume and CRFT 	<ul style="list-style-type: none"> • In Non-shock patients hourly • In shock patients every 15 minutes (until BP is restored)
Hematocrit (HCT/PCV): <ul style="list-style-type: none"> • In uncomplicated DHF • In unstable patients or those with suspected/massive bleeding • Administration of fluid bolus (NS/Dextran-40/blood) 	<ul style="list-style-type: none"> • Every 3 hours • More frequently if necessary • Before and after each fluid bolus
Urine output: <ul style="list-style-type: none"> • Maintained urine output at 0.5-1.0 ml/kg/h (calculated for pre-pregnancy body weight). Preferred UOP in pregnancy is 0.75ml/kg/h 	<ul style="list-style-type: none"> • Measure 3-4 hourly and calculate for every hour.

5.5 GENERAL PRINCIPLES OF FLUID MANAGEMENT IN DHF

5.5.1 FEBRILE PHASE

- Liquids with electrolyte solutions (minimal use of water) at least double the pre-pregnant body weight for one hour - approximately 2,500ml/24 hours (for a maximum body weight of 50kg = 100ml per hour). e.g.: pre pregnant BW 40kg – Fluids 80ml/hr. If unable to take orally, give partly IV.
- Expected urine output could be calculated according to the pre-pregnant body weight (measured 4 hourly): e.g. >50kg pre pregnant body weight woman, urine output should be at least 150ml for 4 hrs (0.75ml/kg/hr).

5.5.2 FLUID THERAPY IN NON-SHOCK DHF PATIENTS DURING CRITICAL PERIOD (ORAL AND IV)

Fluid management in the leaking phase of dengue is of utmost importance. If too little fluid is given during leaking, patient may go into shock and may even die. On the other hand, too much of fluid will lead to fluid overload, which can also lead to death.

- Deciding the onset of the critical phase is very important for fluid management.
- The amount of fluid and type of fluid given at a particular time will depend on
 - the place (how many hours elapsed from the beginning) of the critical phase the patient is on;
 - the amount of fluid used from the total fluid quota up to that time of the critical phase;
 - haemodynamic status and urine output;
 - haematocrit (PCV).
- Once started, plasma leakage gradually increases, reaching a peak usually around 24 hours (around the middle of the critical phase). However, high rate of leaking does not persist for more than a few hours and then it slows down.
- In most patients, the leak is not significant enough to cause haemodynamic instability. Therefore, they would not require much adjustment of the fluid intake.
- However, in some patients the leak can be significant enough to cause haemodynamic instability. Identification of such patients and adjusting fluid intake will prevent them from going into shock.
- Total Fluid Quota (TFQ) should be manipulated according to the patient's haemodynamic status, PCV and UOP as too much fluid could lead to fluid overload and too little fluid can lead to shock.
- Amount of fluid can be gradually increased during the critical phase depending on the need but should be gradually reduced during the latter part of the critical phase
- If the PCV continues to increase or if the patient's haemodynamic parameter/s become abnormal, this indicates significant reduction of intravascular volume.
 - Amount of fluid should be increased in this instance if this happens during the early or middle part of the critical phase. (note: see also the indication for blood transfusion)

- However, if this happens in the second half of the critical phase with increasing PCV, Dextran-40 bolus (500ml over one hour for body weight of 50 kg or more) should be given, provided adequate amount of fluid was given during the first half of the critical phase, and thereafter fluid should be reduced.
- Delayed treatment of intravascular hypovolaemia can result in prolonged shock, leading to organ failure with a high mortality.
- If the patient is haemodynamically stable (non-shock DHF), the TFQ should spread over 48 hours. In a haemodynamically unstable patient (i.e. presenting in shock), TFQ can be given over 24-36 hours.
- Once two thirds of the fluid quota is over, assess the patient's condition to see whether the patient needs continuation of crystalloids, colloid or oral fluids.
- With adequate fluid replacement haemodynamic parameters should be stable and the UOP should be at least 0.75ml/kg/hr.
- Fluid replacement should not be aimed at normalizing the PCV. If the PCV remains around more than 10% of the baseline (e.g. PCV of 33 if the baseline PCV is 30) fluid replacement is adequate provided haemodynamic parameters and UOP are satisfactory.
- If the PCV increases by more than 20% from the baseline, this indicates continuing significant plasma leakage. Such patients need more fluid (or Dextran-40) even if the haemodynamic parameters and UOP are normal.

Calculation of the total fluid quota for a patient during the critical phase:

During the critical phase a measured amount of fluids (both oral and IV) should be given.

- Fluid requirement, both oral and intravenous, in critical phase is **calculated as M+5%** (Maintenance + 5% deficit) using the pre-pregnancy weight (taking maximum weight as 50kg = 4600ml/48hrs). If pre pregnant weight is <50kg calculate TFQ as given below;

M + 5% is calculated as follows:

- | | | |
|----------------------------------|---|----------|
| - For the first 10 kg | - | 100ml/kg |
| - For the second 10 kg | - | 50ml/kg |
| - From 20Kg and above up to 50kg | - | 20ml/kg |

(5% deficit is calculated as 50ml/kg up to maximum of 50kg of pre-pregnancy body weight)

- While it is not necessary to adhere to this fluid volume strictly, one has to keep in mind that exceeding this may lead to fluid overload.

For pregnant women in DHF with pre pregnant body weight ≥ 50 kg, recommended fluid quota during Critical Phase is 4600 ml (both oral and IV) spread over 48 hrs.

Adjusting fluid in DHF:

- If a patient, who is on maintenance fluid volume (e.g. 100 ml/hour), drops the output to less than 0.75ml/kg/hour for 3-4 consecutive hours, increase the fluid volume to 125-150 ml/hour for 3-4 hours. Look for other evidence of plasma leakage. If the output remains low, increase the fluid further to 150-175 ml/hour for the next 2-3 hours. (On the other hand, if the output improves, same fluid volume can be continued for another 2-3 hours and reassess the parameters together with PCV).
 - If the output does not improve with increase of fluid and if the PCV increases, increase the amount of fluid further (to 200-250 ml/hour). However, such high fluid rate should not be maintained for many hours as the patient can get overloaded. If the out-put does not improve with this high rate of fluid, fluid should be changed to a Dextran bolus.
 - If the output does not improve with increase of fluid and if the PCV remains same or decreases, possibility of bleeding and therefore a blood transfusion should be considered.
- Same fluid adjustment can be applied if other haemodynamic parameters become unstable.
- Decision on fluid therapy (adjustments) should be made on vital parameters monitored (pulse pressure/ HR/ BP/ UOP) and capillary haematocrit (PCV)
- Decision to give what type of IV fluid (normal saline/Dextran-40/blood) should be based on inward PCV and quantity of fluid already used.

5.5.3 INDICATION AND ADMINISTRATION OF 10% DEXTRAN-40:

- Signs of fluid overload with high haematocrit:
 - Dyspnea, tachypnea
 - Puffy eyelids, tense/distended abdomen
 - Positive lung signs: crepitation, rhonchi, wheezing

- Persistently high PCV >30% haemoconcentration for >3 - 6 hours despite adequate crystalloid resuscitation.
e.g. if baseline PCV is 35 a 10% rise is 3.5 and therefore 30% rise is $3.5 \times 3 = 10.5$ (A 30% haemoconcentration = $35 + 10.5 = 45.5\%$) Therefore, PCV of >45.5% for 3-6 hrs. is an indication for Dextran-40.

10% Dextran-40 is effective in DHF/DSS patients with severe plasma leakage or those with signs and symptoms of fluid overload because of its hyper-osmolality. It has an osmolality 2.7 times that of plasma and it produces plasma volume expansion by virtue of its highly colloidal starch structure. Dextran-40 is a plasma expander and can hold the volume better than crystalloid and other colloids that are iso-oncotic to plasma. Other colloidal solutions including Fresh Frozen Plasma (FFP) and 5% Albumin are in the plasma substitution group (osmolality = plasma); therefore, is not effective and will worsen fluid overload.

How to give Dextran-40 *

Dextran-40 is given as a bolus only during the critical phase of DHF and volume should be added to the total fluid quota (M+5%).

- Always give in a bolus dose:
 - 10 ml/kg/hr in <50kg pre pregnant weight
 - 500 ml/hr in ≥ 50 kg pre pregnant weight at a time
- Do PCV before and immediately after Dextran bolus
 - If PCV drops > 10 points, consider significant bleeding
 - If PCV drops below baseline, consider bleeding
- Maximum dose
 - 30 ml/kg/24 hrs in <50kg pre-pregnant woman
 - 1,500 ml/24 hrs in ≥ 50 kg pre-pregnant woman

*Source: Professor Siripen Kalayanaroj (MD), WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, Bangkok, Thailand.

Clinical and laboratory parameters indicating adequacy of fluid resuscitation/therapy

- Clinical parameters:
 - Improvement of general well-being / good orientation & mental state
 - Warm peripheries with CRFT ≤ 2 sec
 - Adequate urine output (>0.75 ml/kg/hr)
- Vital signs and biochemical parameters:
 - Stable BP with maintaining pulse pressure more than 30mmHg
 - Reduction in tachycardia or normalization of heart rate
 - Reducing tachypnea or normalization of respiratory rateImprovement in metabolic acidosis and lactate levels (20% decrease in two hours improves survival)
- HCT/PCV:
 - Decrease in HCT (in the face of haemodynamic stability)

5.6 CHALLENGES IN RECOGNITION OF PLASMA LEAKAGE IN PREGNANCY

- Hyperemesis during first trimester of pregnancy resembles warning signs of leaking which may delay the recognition of DHF.
- The lower baseline HCT after the second trimester should be noted. Establishing baseline hematocrit (by doing FBC) during the first 2 days of fever is essential for early recognition of plasma leakage (to detect rising towards 20%).
- During pregnancy wide pulse pressure (PP) may delay the detection of **compensated shock** (consider PP ≤ 25 mmHg as cut off point), and low baseline BP may delay the detection of **hypotensive shock**.

CHAPTER 6 : PARTURITION MANAGEMENT IN DENGUE

In a pregnant woman with dengue illness in labour, delivery should take place in a hospital where a team comprising of Obstetrician, Physician, Paediatrician/Neonatologist, Anaesthetist/Intensivist (Multi-Disciplinary Team) and blood/blood components are available.

6.1 TIMING AND MODE OF DELIVERY

Outcome of dengue illness in late third trimester, particularly if a woman is in labour, can be unfavorable unless the delivery is planned properly.

In view of possible high mortality as a consequence of delivery it is advisable to;

1. Avoid Induction of labour or elective Caesarean section during the critical phase of the illness. It is best to delay until the critical phase is over and the patient reaches recovery phase. However, if the delivery is inevitable, delay it until the platelet count resumes to recover and increase to over $50 \times 10^9/L$ (occasionally, therapeutic platelet transfusions may be needed before intervention).
2. If premature labour occurs during critical phase, it is advisable to delay the delivery until the leaking resolves by using **tocolytic drugs** such as Nifedipine or Atosiban (Atosiban is an FDA approved oxytocin receptor antagonist currently not available in Sri Lanka). **In a normotensive patient Nifedipine does not reduce the blood pressure significantly.** The most commonly used regimen for acute tocolytic treatment is 20mg of Nifedipine initially, and if contractions persist and no hypotension, followed by another 20mg 30 minutes later. Followed up with 20mg 8 hourly (Avoid in cardiac disease and hypotension with BP less than 90/50mmHg, cautioned in tachycardia). Due to vasodilatation induced by Nifedipine maternal monitoring should be intensified.
3. If it becomes mandatory or indicated, the delivery, by Induction of labour or a Caesarean section, may be considered during early febrile phase of the illness before the onset of critical phase when the platelet count is above $130 \times 10^9/L$. It is recommended to make this decision by the multi-disciplinary team (MDT). In such an instance, indication and reasons for delivery should be well documented.

4. During the critical phase vaginal delivery or Caesarean section should be undertaken only if the mother's life is at risk or the patient develops spontaneous labour during this period. If there is a foetal indication (Foetal Distress) for delivery, it is recommended not to intervene and deliver during critical phase. Patient and relatives must be counselled about the risk to pregnant woman's life if intervened at this time (either by Induction or Cesarean section). This decision should be taken by the multi-disciplinary team and indication and reason for nonintervention should be well documented.

AIM OF TIMING AND MODE OF DELIVERY

Irrespective of the outcome for the baby, priority should be given to saving the mother's life.

- Pregnant women should be monitored closely for vital signs and bleeding while close continuous foetal monitoring is required to detect foetal compromise.
- Blood grouping and cross matching must be done for all dengue patients anticipating labour.
- Normal/instrumental delivery in these patients should be conducted under close supervision of the Obstetrician.
- Majority of patients can be allowed to progress to spontaneous vaginal delivery in the convalescent (recovery) phase. Elective delivery is best avoided in diagnosed Dengue patient until patient recovers with a platelet count $>50 \times 10^9/L$.
- Intense active management of third stage of labour in preventing postpartum haemorrhage is required by the use of IV **uterotonic agent**. Follow the National Obstetric Guideline regarding active management of third stage of labour. Since this is a high-risk situation, give **05 IU of Oxytocin slow IV bolus** (No IM injections due to bleeding tendency in Dengue). This should be followed by oxytocin 10 IU per hour as a concentrated infusion – standard follow up infusion can cause fluid overload. Alternatively Misoprostol (800micrograms) could be used rectally. Ergometrine is best avoided in women with hypotension in DHF (vasoconstriction caused by it can worsen visceral ischaemia).
- In NVD or LSCS it is advisable to replace the estimated blood volume lost concomitantly. In such patients it is important to monitor vital parameters and haematocrit (PCV) frequently until stable.

6.2 RISK OF COMPLICATIONS IN PREGNANT WOMEN BY OPERATIVE INTERVENTIONS

Phases of illness	Before illness	Febrile phase (1 st 3 days)	Critical/leaky phase (48h following febrile phase)	Convalescent phase	After Recovery
Clinical and laboratory findings		<ul style="list-style-type: none"> • Fever, headache, myalgia • Low WBC • PLT >130x10⁹ • Normal HCT • No evidence of fluid leak 	<ul style="list-style-type: none"> • Rising WBC >5,000 • PLT dropping <130x10⁹/L • Rising HCT • USS evidence of fluid leak 	A – Appetite Improved B – Bradycardia C – Convalescent Rash /Itching D – diuresis WBC normal PLT rising >50x10 ⁹ /L PCV normal	
Risk category		MODERATE TO HIGH-RISK	VERY HIGH-RISK	MODERATE RISK	
Place of management		Pre op: Ward Post op: HDU/ICU	(HDU/ICU) Level II-III critical care	(HDU/Ward) Level 1-11 Critical care	
Specific Ix before delivery & operative intervention		<ul style="list-style-type: none"> • NS1Ag • PLT • Hb, HCT • USS - abdomen & chest 	<ul style="list-style-type: none"> • NS1Ag and IgM • PLT, Hb, HCT • Coagulation, ROTEM • USS - abdomen & chest • SGOT/SGPT 	<ul style="list-style-type: none"> • IgM/IgG • PLT, Hb, HCT • Coagulation, ROTEM • SGOT/SGPT 	
Specific precautions before operative intervention		<ul style="list-style-type: none"> • MDT discussion 	<ul style="list-style-type: none"> • Correct PLT >50x10⁹/L • Correct deranged coagulation (ROTEM) • Correct Hb >10 • Optimize organ function • Be ready to manage major post- partum haemorrhage, DIC • MDT discussion 	<ul style="list-style-type: none"> • Correct PLT >50x10⁹/L • Correct deranged coagulation • Correct Hb >10 • Be ready to manage PPH • Beware of sepsis in the presence of IUD • MDT discussion 	

Management following multi-disciplinary team (MDT) discussion

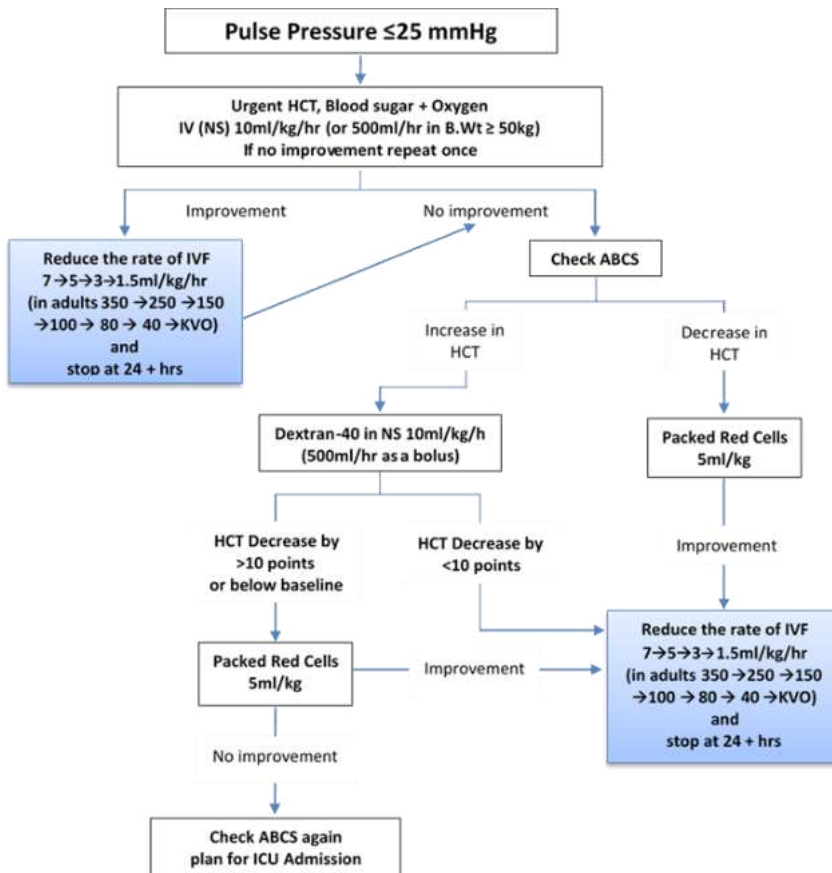
	Risk category	Possible indications for Caesarean section during Dengue illness
	Moderate risk Early febrile phase High-risk Late febrile phase	First 2 days of fever with $PLT > 130 \times 10^9/L$ and no USS evidence of fluid leak: <u>Foetal</u> - Late foetal heart rate decelerations during labour, evidence of foetal hypoxia <u>Maternal</u> - Past CS in labour Bleeding placenta praevia even without hypovolaemia Failed instrumental delivery 3rd day of fever when $PLT < 130 \times 10^9/L$, but no USS evidence of fluid leak: Only to save the mother's life - e.g. significant placental abruption, maternal cardiorespiratory distress due to a cause other than Dengue
	Very high-risk Critical phase	Only to save the mother's life (e.g. significant placental abruption, maternal cardiorespiratory distress due to a cause other than Dengue)
	Moderate risk	Foetal compromise Maternal compromise, deteriorating but compensated maternal medical condition, postponed CS during febrile or critical phase
	Normal risk	operation at short notice but no clinical urgency and elective CS

CHAPTER 7 : MANAGEMENT OF COMPLICATIONS OF DHF DURING PREGNANCY

Common complications of DHF both in pregnant and non-pregnant women are seen as a result of **prolonged shock** and **fluid overload**. Due to prolonged shock as a consequence of **inadequate fluid therapy** and **failure in aggressive resuscitation**, the patient may develop **heavy bleeding** and **multi organ dysfunction**. Fluid overload is commonly due to inappropriate fluid therapy not guided by monitoring parameters resulting in respiratory distress requiring ventilation.

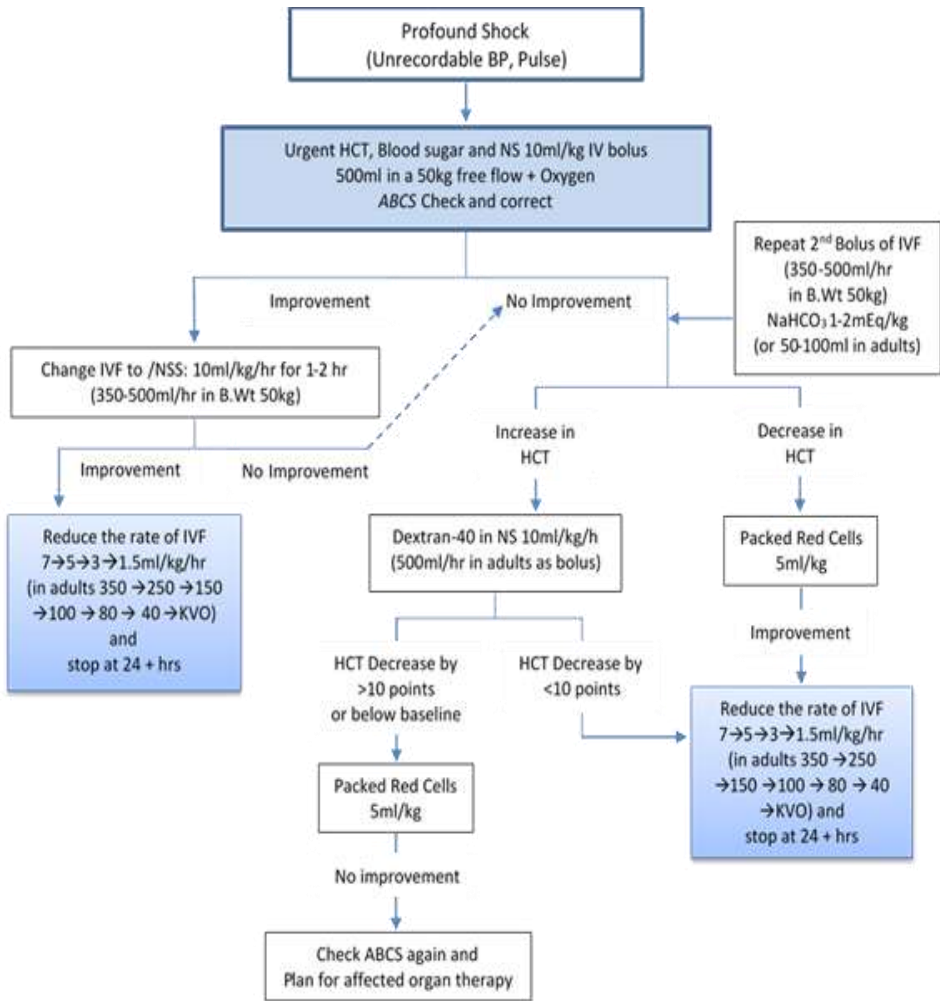
7.1 MANAGEMENT OF SHOCK

7.1.1 IV FLUID THERAPY FOR DHF WITH COMPENSATED SHOCK IN PREGNANCY



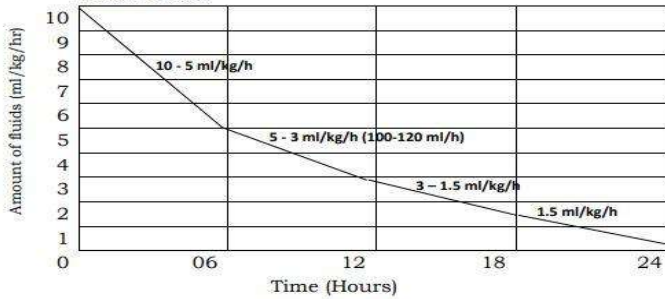
Source: Professor Siripen Kalayanaroj (MD), WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, Bangkok, Thailand.

7.1.2 IV FLUID THERAPY FOR DHF WITH DECOMPENSATED SHOCK IN PREGNANCY



*

Guide for the rate of IV fluids in profound shock after initial resuscitation



Source: Professor Siripen Kalayanaroj (MD), WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, Bangkok, Thailand.

Above figure gives suggested IVF therapy in DHF with shock (DSS) over a period of 24 hrs+. IVF is recommended for 24 hrs+ when a patient presents in shock. Patient should be resuscitated and followed according to the flow chart above with gradual reduction of fluid rate.

If, stable clinical condition, vital signs and urine output are not achieved with the above fluid therapy, consider complications (**A** - Acidosis, **B** - Bleeding, **C** - Calcium, **S** - Sugar + **F** – fluid overload). If the patient has acidosis ($\text{pH} \leq 7.35$ with $\text{HCO}_3^- < 15 \text{mmol/l}$) it indicates **prolonged shock** and such patients are likely to have organ(s) involvement (possible liver and kidney injury). Correct acidosis quickly, preferably with a bolus of NaHCO_3 1ml/kg. Follow up with another 1ml/kg if response is inadequate. Correcting acidosis quickly will reduce the occurrence of DIC. DIC will result in massive bleeding and advanced DIC will develop quickly in acidotic environment.

7.2 MANAGEMENT OF BLEEDING

Bleeding is common in dengue illness. This can range from petechial haemorrhages to life threatening bleeding. In adults, clinically significant bleeding can occur in DF, DHF with shock and in DHF without shock. As such, bleeding is an important complication in pregnant dengue patients. Furthermore, if the patient delivers during the illness, bleeding is likely to be more due to oozing from raw uterine surface. Surgical manoeuvres, including LSCS, can result in severe, life threatening bleeding and should be avoided in critical phase of DHF unless to save mother's life.

7.2.1 DETECTION OF BLEEDING.

Overt bleeding can manifest as bleeding per vagina or haematemesis. However, significant bleeding could be often **concealed**. Such bleeding can occur into GI tract (manifest later as melaena), muscles, abdominal cavity or thoracic cavity and brain.

During dengue illness early bleeding should be anticipated if the patient has been on NSAIDs, Aspirin and steroids.

Features of haemodynamic instability, together with reduction of HCT or absence of rise in HCT indicate possible bleeding. Although tachycardia may not be always present with bleeding, tachycardia without fever suggests the possibility of significant bleeding.

Suspect bleeding if;

- Any of the haemodynamic parameters become abnormal (e.g. tachycardia disproportionate to fever, prolonged CRFT, reduction of UOP) with reduction of HCT.
- Any of the haemodynamic parameters become abnormal (e.g. tachycardia disproportionate to fever, prolonged CRFT, reduction of UOP) without a rise in the HCT (equivocal).
- When patients present with shock, especially hypotension, postural hypotension, dizziness, fainting but no adequate rise in HCT. Further, in these patients AST/ALT will be elevated >200 IU/L (Can be >1000 IU/L).
- Significant increase in WBC count (neutrophil leucocytosis) with reappearance of fever can be due to **Bleeding**, **Bacterial infection** and **Hepatitis (BBH)**.
- Tachycardia (>110/min) without fever
- Drop of HCT >10 points following a bolus of Dextran-40 (administered 10 ml/kg/ hr)
- Sudden fall of HCT below baseline (following fluid resuscitation in shock)

7.2.2 TREATMENT OF BLEEDING.

Treatment of bleeding is volume replacement with blood. Until blood is available, fluid should be transfused: crystalloids in early or middle of the critical phase and Dextran-40 in the latter part of the critical phase. If the patient is unstable, blood should be given rapidly. After the transfusion, haematocrit (HCT) should be repeated.

Even if bleeding is likely and haematocrit is >45% do not give blood without bringing down the HCT first by giving a colloid (Dextran-40, 10ml/kg/hr).

- Volume of blood transfused should not be added to total fluid quota during the leaky phase.

- Threshold for blood transfusion is low in dengue with pregnancy. Packed Red Cells (PRC) 5ml/kg can be given at a time. HCT is expected to rise by 5 points (e.g. from 30% to 35%) with this amount of blood.
- Immediately after the baby's delivery (end of the second stage of labour), the cervix and vagina should be thoroughly inspected for lacerations and surgical repair should be performed early.

Clinical tip: Guidelines for visual estimation of blood loss

- 60ml: small 10×10cm swab (maximum saturated capacity)
- 140ml: medium 30×30 cm swab (maximum saturated capacity)
- 350ml: large 45×45cm swab (maximum saturated capacity)
- 500ml: 50cm diameter floor spill
- ❖ Excessive vaginal bleeding—soaking a pad in an hour

If the patient had NVD or LSCS it is advisable to replace the estimated lost blood volume immediately. It is essential to monitor haematocrit and haemodynamic parameters frequently in such patients as they are likely to have continuous bleeding and may need further blood transfusions.

7.2.3 ABSOLUTE INDICATIONS FOR BLOOD TRANSFUSIONS

- Overt blood loss of 250-300 ml
- Drop in haematocrit without clinical improvement despite adequate fluid replacement.
- A drop in haematocrit of >10 points after Dextran-40 (given as 10 ml/kg or 500 ml bolus)
- Dengue shock not responding to adequate fluid therapy i.e. 40-60 ml/kg (Refractory shock)
- Hypotensive shock with low or normal haematocrit
- Persistent or worsening metabolic acidosis despite adequate fluid replacement

7.2.4 CONSIDER BLOOD TRANSFUSION

1. If the patient is in shock but haematocrit (HCT/PCV) rise is not high enough as expected for the degree of leak leading to shock
2. Low or normal PCV with unstable haemodynamic parameters such as; cold clammy extremities, prolonged CRFT, tachycardia, narrow pulse pressure (25-30 mmHg), and reduced UOP.
3. Increased INR (liver failure) with low PCV
4. Anaemia in pregnancy – Pregnant women with low haemoglobin (Hb \leq 8g/dl) e.g. Iron Deficiency, Thalassemia Minor, with dengue illness, blood transfusion should be considered early.

7.2.5 PLACE FOR PLATELET TRANSFUSION

1. Low platelet count is not an indication for prophylactic platelet transfusions as there is no relationship with bleeding and low platelet count (without trauma).
2. If VD progressing in spite of tocolytics or if LSCS is essential (to save mother's life) platelet transfusions would be necessary to keep the platelet count $>30 \times 10^9 - 50 \times 10^9/L$ respectively.
3. If the patient continues to bleed in spite of several blood transfusions, there is a place for therapeutic platelet transfusions.
4. Platelet transfusion may be indicated in the presence of heavy overt bleeding with low platelet counts.
5. Insertion of central venous catheter for continuous renal replacement therapy (CRRT) – aim at platelet count of $>30 \times 10^9/L$.

7.2.6 PLACE FOR TRANSFUSION OF OTHER BLOOD PRODUCTS.

1. If the patient develops liver failure, platelet, FFP and cryoprecipitate would be indicated. However, clinicians have to be conscious of the possible fluid overload with platelet and FFP transfusions.
2. Factor VII may have a place only if the bleeding is from a single point (e.g. Gastric ulcer)
3. Prothrombin concentrate complex (containing factors II, VII, IX, X) may have a place in bleeding with liver failure.
4. For significant bleeding, ROTEM/TEG guided coagulation management is given in *Annexure 3*.

7.3 INDICATIONS FOR OTHER ADJUNCT THERAPY

Calcium Gluconate – 10% calcium gluconate 10ml over 10 minutes is justifiable if a patient is in shock and is not responding to adequate fluid replacement. This may be continued 6 hourly for 24-36 hours.

Hypoglycaemia - if blood glucose level is <70/mg/dl correct it by giving 25-40ml of 25% dextrose intravenously. Recheck in 15 minutes and repeat.

7.4 MANAGEMENT OF MULTI-ORGAN FAILURE

- Hepatic failure / Renal failure / Respiratory failure / Encephalopathy / Encephalitis: manage according to the standard protocol/guidelines.
- Myocardial involvement: bedside echo cardiogram can assess cardiac function. Continue fluid replacement (do not restrict fluid).
- Other complications – electrolyte imbalance, co-infections should be managed according to standard protocols.

7.5 ABSOLUTE INDICATIONS FOR ICU ADMISSION

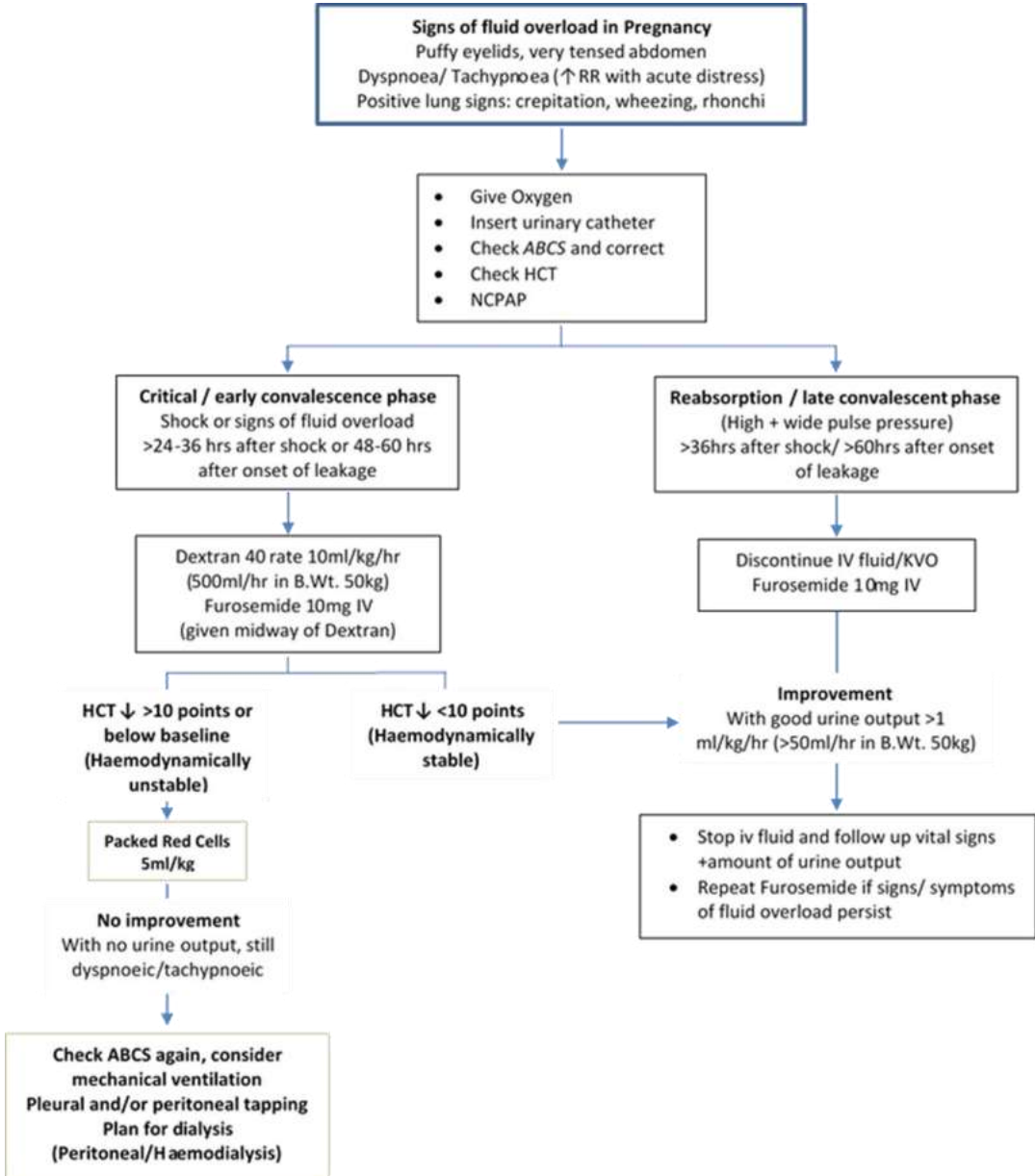
- Severe plasma leakage leading to shock and/or fluid accumulation with respiratory distress
- Severe bleeding
- Severe organ impairment
- Following inevitable surgical interventions done on a patient in critical phase
- A parturient in critical phase

Indications for intubation and ventilation are:

- Acute respiratory failure (ARDS)
- Severe cardiovascular instability
- Severe metabolic derangement (raised lactate > 10mmol/L)
- Altered mental state

7.6 MANAGEMENT OF FLUID OVERLOAD

Use of excess fluids or fluids given beyond the time of plasma leakage are the usual causes of fluid overload.



Source: Professor Siripen Kalyanarooj (MD), WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, Bangkok, Thailand.

7.7 SPECIAL OBSTETRIC CONDITIONS AND DENGUE HAEMORRHAGIC FEVER

7.7.1 HELLP SYNDROME (*Haemolysis, Elevated Liver enzymes and Low Platelets*)

- In pre-eclampsia and HELLP syndrome, thrombocytopenia is a common feature. Assess with serial FBC, NS1 Ag and Dengue IgM in a patient with a history of fever to exclude dengue.
- In some pregnant women with gestational thrombocytopenia, PLT count is $\leq 150 \times 10^9/L$. PLT count is low in HELLP syndrome; very low PLT count $< 30 \times 10^9/L$ is rarely seen in HELLP.
- If initial FBC is suggestive of Thrombocytopenia follow up with serial FBC to exclude dengue.

Comparison between HELLP syndrome and DHF

	CLINICAL FEATURES FOR DIAGNOSIS	HAEMATOLOGICAL FINDINGS	BIOCHEMICAL FINDINGS	MANAGEMENT
HELLP syndrome	<ul style="list-style-type: none"> • Evidence of pre-eclampsia • Haemolysis • Elevated liver enzyme • Low platelet counts • H/o flu like illness 	Blood picture (MAHA) Thrombocytopenia	AST and ALT both raised > 70 IU/L Elevated LDH > 600 U/L	Termination of pregnancy
DHF	<ul style="list-style-type: none"> • Fever/history of recent fever • Bleeding tendency • Thrombocytopenia Evidence of plasma leaking identified with ultrasonography	Leukopenia Thrombocytopenia (often $< 50 \times 10^9/L$) Hematocrit rise (towards 20%)	In complicated DHF AST markedly elevated than ALT and shows rapid rise	Delay delivery until the end of critical phase

7.7.2 DETECTION AND MANAGEMENT OF COMPLICATIONS DURING POST-PARTUM PERIOD

- Risk of PPH is higher in instrumental delivery, surgical interventions and pregnancy related conditions (multi gravida, placenta previa, etc.).
- Fever during the post-partum period due to acquired dengue infection may be misdiagnosed as puerperal sepsis.

- Newborns with mothers who had dengue just before or at delivery, should be closely monitored and investigated in hospital after birth, up to a week in view of the risk of vertical transmission.
- Oxytocin infusion should be commenced to contract the uterus after delivery to prevent postpartum hemorrhage. Misoprostol may be given for PPH as prophylaxis/treatment.
- Ensure no retained placenta
- It is estimated that 300-500ml blood enters the circulation with uterine contractions. However, soon after delivery transfuse the estimated blood loss early.
- After every LSCS, estimated blood loss should be replaced.
- Give Tranexamic Acid 1g slow IV after delivery by LSCS or NVD at the time of blood transfusion.

7.7.3 MANAGEMENT IN THE PRESENCE OF AN INTRAUTERINE FOETAL DEATH

The occurrence of intra uterine foetal death (IUD) is rare in Dengue infection of a pregnant woman. However, it is a known complication in the 3rd trimester.

- Diagnosis of IUD requires appropriate and urgent assessment using real-time ultrasound. Do not diagnose foetal death only based on absence of foetal heart on auscultation or by hand-held Doppler.
- Delivery of IUD could be delayed by at least 1 week, if the patient is physically well with intact membranes and there is no evidence of infection, preeclampsia or bleeding (including laboratory evidence of DIC).
- If there is evidence of infection, IV antibiotics should be started.
- If labour is delayed for >48hrs, testing for DIC should be done twice weekly or more frequently as necessary.

7.7.4 MANAGEMENT OF PERINATAL AND VERTICAL TRANSMISSION OF DENGUE

Perinatal dengue infection is the result of vertical transmission from mother to offspring. A study in French Guiana (1992 – 2006) has shown 15% vertical transmission in 53 pregnant dengue patients.

In general, dengue infections in the newborn babies are usually mild and DF is more likely. Fever is the initial presentation in most babies, commonly on 4-5 days after birth or even on day 01 of birth or later than 6 days. Therefore, suspected neonate should be observed at least for 1 week for evidence of vertical transmission. Other clinical presentations are petechiae, rash and hepatomegaly. Convulsions (may mimic CNS infection) and diarrhoea are common unusual presentations. In early febrile phase leucopenia may not be found as leukocytosis is common in early infancy.

Neonates have less respiratory reserve and they are more susceptible to liver impairment and electrolyte imbalance (prone to get hyponatraemia). If they develop DHF, duration of plasma leakage is shorter (usually 12 – 24 hrs.). As leucopenia is not common, increased haematocrit (possibly with ultrasound evidence) and thrombocytopenia will help clinical diagnosis of DHF.

In the management of DHF in neonates optimum fluid therapy from the onset of entry into the critical phase is vital for good outcome. Baby should be evaluated frequently for oral fluid intake (i.e. breast feeding) and urine output (hence early need for catheterization). As IVF, half normal saline (N/2 in 5% Dextrose) should be given. If high rate of crystalloids are required (N/2 + 5% Dextrose) following fluid resuscitation with crystalloids, colloids (10% Dextran 40) should be considered. They may respond quickly to fluid resuscitation. Therefore, they should be monitored more frequently for fluid requirement and urine output.

Fluid overload is common in neonates due to less chest compliance. If IVF are continued beyond leakage phase it will easily lead to fluid overload. Breast feeding in neonates with DHF can lead to fluid overload if not cautious. Further, if liver enzymes are elevated to a level of liver failure or impending liver failure, breast feeding may have to be temporarily withheld as proteins in the gut could worsen liver failure.

Chapter 8 : NURSING CARE DURING PREGNANCY, COUNSELLING OF PATIENT/ FAMILY, AND THE CONVALESCENT (RECOVERY) PHASE

8.1 NURSING CARE

All nurses stationed in ETU, OPD, Medical, Obstetric units and ICU need to have basic knowledge on natural course of DF/DHF/DSS.

Nurses should develop necessary skills to identify the correct phase of DHF/DSS in pregnant women so that appropriate and proper monitoring can be provided for the individual patient.

8.1.1 GENERAL IN-WARD CARE

- Ensure availability of essential equipment in working order – Micro-haematocrit machine and Multi-monitors.
- Order and stock essential drugs – including 10% Dextran-40
- Maintain mosquito free environment
- Provide essential information to both patient and by-stander on dengue management at the time of admission and give psychological support regularly
- Collect and send blood for laboratory investigations on time and trace reports promptly
- Notify Medical Officer of Health (MOH) where patient has resided two weeks prior to illness

❖ Febrile Phase

1. High fever, Headache, Arthralgia, Myalgia

- Maintaining QHT chart. Inform doctor when fever is settling or afebrile.
- Observe for tachycardia (which is disproportionate to fever) or even without fever.
- Give Paracetamol when temperature is ≥ 39 °C.
- Apply warm water compress / tepid sponging.
- Adequate fluids – Avoid plain water.

2. Anorexia, Nausea and Vomiting

- Provide & encourage the patients to have soft balanced nutritious diet – Avoid red, black, brown coloured food.

- Severe vomiting, look for signs of dehydration.
- Give antiemetic with the doctor's instructions. They may need intravenous fluids.
- Provide clean, transparent container with a lid to collect & measure vomitus of patients.

3. Abdominal Pain

- Help the patient to lie down or to be in a comfortable position.
- Provide soft, clean, dry and comfortable wear.
- Avoid tight contacts with abdomen.
- Peptic ulcers are a common reason for abdominal pain. Give medication according to doctor's instructions; e.g. Ranitidine, Famotidine

4. Bleeding (eg. Epistaxis, Hematemesis, Bleeding from gums, PV bleeding)

- Notify on-call doctor
- Estimate and record the amount of blood lost (eg. no. of soaked sanitary pads)
- Arrange blood for DT.
- Avoid intra-muscular injections.
- Venepuncture - apply pressure to the site with sterile gauze.
- Epistaxis – apply an ice pack or nasal packing.
- Gum bleeding – tooth brush is not recommended. Clean the oral cavity softly with a cotton bud.
- GI Bleeding - observe vital signs closely & check PCV. Record colour of stools for possible GI Bleeding & Melaena
- NG tube insertion is contraindicated as it may trigger severe bleeding by trauma.

Always maintain an accurate DENGUE MONITORING CHART

❖ Critical phase

Indications to call for immediate advice

- Pulse rate > 120/min with fever or >100/min without fever.
- Pulse Pressure 30-25 mmHg or less (in left lateral position)
- Postural drop of SBP >20mmHg.
- Significant bleeding (Haematemesis, Melaena, Bleeding PV etc.)
- UOP <0.75ml /kg/hr
- CRFT > 2 sec

- Manage the patient in ward HDU (close to nurses' station).
- Regular monitoring according to Guidelines (preferably hourly) Critical Phase Monitoring Chart – Annexure 2

- Recognize abnormalities of the vital parameters and inform on-call doctor early.
- Perform investigation as instructed and trace the report promptly.
- Preparedness and availability of medication in ward HDU (make sure essential medication and IV solution including Dextran-40 are readily available inward)
- Trace lab reports and inform doctor.
- Strictly adhere to management protocols given by the doctor on fluid therapy (rate of fluid infusion)
- Perform and monitor inward PCV, especially before and after fluid bolus.
- Provide instant care - assist during dengue emergency resuscitation (e.g.: Dengue shock)
- Detect respiratory distress early – count RR, look for tachypnoea and dyspnoea

❖ **Convalescent phase**

- Recognize signs and symptoms indicating recovery.
- Monitor vital parameters according to the need.

Advice before discharge

- Advice to take adequate rest
- If platelet count is low to avoid strenuous exercises.
- Explain that they can now engage in normal day-to-day activities.
- To clean the immediate environment.

8.2 PATIENT COMMUNICATION

The importance of establishing a good relationship with the patient, husband and other family members from the time of admission cannot be over emphasized. This can be easily established by good communication between the medical staff and the patient.

This should involve the following;

1. Discussion about the nature of the illness, natural course, possible outcomes and treatment options.
2. Information should be given regarding favourable outcomes of dengue, with appropriate management. However, information must also be given regarding the complications and

mortality in the event of dengue illness being complicated by severe dengue shock syndrome complicated by multi organ failure, in simple language.

3. Study the patient records (BHT) well before discussions are commenced. In particular note the platelet count, PCV, urine output and blood pressure, as the patient and the relatives too would be well aware of the latest information.
4. Document every discussion made with the patient and the family in the BHT.
5. Explain that the patient is under the care of a multi-disciplinary team of experts comprising of obstetricians, physicians, paediatricians, anaesthetists etc. and that the best possible management is being done according to national guidelines for the safe delivery of the mother and the baby.
6. Explain that the mode of delivery whether by vaginal or by Caesarian section will be judged, depending on the duration of pregnancy, the state of the dengue illness and the condition of the mother, in the best interest of both mother and baby.
7. Reassure the patient, husband and family members that dengue complicating pregnancy is not fatal and safe delivery of the baby can be ensured.

8.3 BREAKING BAD NEWS

8.3.1 MATERNAL DEATH

1. Death of a mother from dengue or any other cause is a devastating experience for the entire family, especially the husband and the remaining children.
2. If the condition of the pregnant mother with dengue was hopeless from the start, the relatives should have been informed by the medical professionals about the poor prognosis and the possibility of death from the very beginning.
3. If the death occurred unexpectedly, explain that everything possible was done to prevent this catastrophe and that the present situation was unfortunate and unavoidable. The family should be reassured that all measures and possible treatment options were utilized to save the mother, despite the unexpected turn of events.
4. Provide psychological and emotional help to the family by trained counsellors.

8.3.2 DEATH OF THE BABY

Explain that everything possible was done in the best interest of the mother and the baby, with the concurrence of the neonatologists and the obstetricians. However, if the baby had died due to early termination of pregnancy, explain that this decision was made reluctantly to save the life of the mother.

8.4 CONVALESCENT (RECOVERY) PHASE

Recovery Phase starts after the end of the critical phase and usually lasts for 2-3 days. Reabsorption of the extravasated fluid is seen during this period.

8.4.1 SIGNS AND SYMPTOMS OF RECOVERY

- Improved general well-being and improved appetite
- Urine output will be normal or increased (diuresis)
- Haemodynamic stability (normal BP and Pulse)
- Haematocrit returns to baseline (may even be lower than baseline due to fluid reabsorption)
- Rise in white cell count followed by a sustained rise in the platelet count
- Bradycardia, appearance of convalescent rash, generalized itching (more intense in palms and soles) may be seen in some patients.

8.5 DISCHARGE CRITERIA

The following criteria are to be taken into account while contemplating a discharge of a dengue patient

- Afebrile for 48 hours (without antipyretics)
- Stable general condition
- Recovery of appetite
- Stable haematocrit for at least 24 hours
- Rising trend in platelet count $>50 \times 10^9/L$ (at least two counts done within 12 hours apart)
- No dyspnoea or respiratory distress attributable to pleural effusion or ascites

8.6 ADVICE ON DISCHARGE

- Advise to take rest at home for 1 week avoiding traumatic activities or procedures.
- There is no risk of spread of dengue virus now and patient can go back to work.
- If anyone in the same household gets high fever they should seek early treatment.

CHAPTER 9 : CHALLENGES IN DIAGNOSIS AND MANAGEMENT DURING PREGNANCY

9.1 MANAGEMENT DELAYS

There are three levels of management delays that may result in an adverse clinical outcome: (1) delay in presentation to the health care system resulting in delayed admission and hence delayed institution of appropriate rehydration, (2) delay in instituting appropriate rehydration measures in hospitalized patients, and (3) delay in discontinuing rehydration towards the end of the critical phase resulting in fluid overload and iatrogenic death.

(1) Delay in presentation to the health care system: the root cause is often lack of community awareness leading to late health care seeking behaviour of patients with febrile illnesses including dengue. Therefore, the strategy is to increase community awareness about dengue. The message to the public is that all patients with acute febrile episodes need to seek early medical attention. In addition, the public needs to be aware that the critical phase often starts at the end of the febrile phase.

(2) Delay in institution of rehydration measures at hospital-level: the root causes include slow laboratory processes in obtaining laboratory results, non-streamlined work processes leading to delayed attention of the clinicians in-charge, lack of access to resources to make a prompt diagnosis of capillary leakage (such as serial haematocrit measurements, ultrasound etc.), and untrained personnel. The strategy entails improving rapid access to laboratory results such as platelet count, haematocrit, and clinical assessments including blood pressure, urine output, fluid accumulation as assessed by ultrasound etc. It also entails a well-planned work flow between junior and senior doctors, between emergency room, outpatient department and inpatient wards, and a dedicated high dependency ward with special attention to the care of dengue patients with capillary leakage. Delay in adequate fluid resuscitation is a major concern with under perfusion of patients in shock.

(3) Delay in reducing/restricting fluid therapy: the root cause is usually lack of training and experience in managing dengue patients during the critical phase. The result is over-hydration of patients, at a time when reabsorption of fluids occurs towards the end of the critical phase, which leads to fluid overload and sometimes, death. The strategy includes better training and monitoring of clinicians treating complicated dengue cases, careful audits of fatal cases to learn from any mistakes made, and setting up dedicated high dependency units (HDU).

9.2 STEPS TO MINIMIZE MANAGEMENT DELAYS

Five essential steps are required in proper clinical management of dengue patients to reduce fatal outcomes: (1) early diagnosis and indication for admission, (2) early detection of plasma leakage and time-sensitive institution of fluid rehydration, (3) Investigations and correction of common complications in patients who do not respond to conventional IV fluid therapy, (4) early detection of bleeding and early blood transfusion, and (5) early diagnosis of cases with unusual manifestations, especially those with encephalopathy, co-morbidity and co-infections.

By reviewing the processes of dengue case detection and clinical management, gaps in all 5 steps of clinical management can be identified. However, the main cause of death is fluid overload. The main reason for death is not failure to diagnose early, but clinical management of shock with a tendency to over-hydrate over a longer period than required. Delayed blood transfusion and delays in transferring patients to tertiary care facilities with high dependency wards (HDUs) are additional factors.

Chapter 10 : CASE STUDIES IN CLINICAL MANAGEMENT AND SUGGESTED IMPROVEMENTS FOR PREGNANT WOMEN

Table: Steps in clinical management, common findings and suggested improvements

Steps in Clinical Management	Common Findings (Issues)	Suggested improvements
1 Early clinical diagnosis of dengue and indication for admission	Early diagnosis by NS1 Ag done, but not admitted properly. More than half admitted early but received too much IV fluid.	Admit during early febrile phase. Assess patients using duration of Fever, Warning Signs, Vital Signs and FBC. Diagnose DHF early and manage accordingly
2 2.1 Early detection of plasma leakage	Plasma leak detected too late or overlooked. Patients develop shock/ profound shock while in hospital	Check FBC regularly as PLT drops; Repeat HCT when PLT drop $<130 \times 10^9/L$ Use USS effectively to detect leaking
2.2 Proper IV fluid management	Giving too much IV fluid for too long. Giving too little fluids Resuscitation in shock not aggressive enough	Initially use 3 hrly febrile phase monitoring chart and give measured amount of fluid. When leaking starts change over to Critical phase chart and monitor hourly or more often while giving fluid (both IV and Oral). Stop IV when leaking is over
3 Investigations and correction of common complications if patients do not respond to conventional IV fluid therapy (cannot reduce the rate of IV fluid)	Not investigate and correct common complications in DHF Do not anticipate complications when patient not improving with standard IV therapy	Check and correct; A – Acidosis B - Bleeding C – Calcium S – Sugar F – Fluid Overload
4 Early detection of bleeding and early blood transfusion	Delayed blood transfusion found in half of fatal case	Disseminate list of common indications for blood in Dengue
5 Early diagnosis of cases with unusual manifestations, especially those with encephalopathy, co-morbidity and co-infections	Rare due to dengue virus itself Usually seen as a consequence of prolonged shock	Look for complications and treat accordingly

10.1 CASE - #1

A 35 year old previously healthy woman married for 6 months who missed her past regular period was transferred from a peripheral hospital for specialized management of suspected ectopic pregnancy.

History: She had fever for 4 days. Complained of faintishness and abdominal pain on the day of transfer. She had no peripheral pulse, Low BP, patient conscious & rational (GCS 15/15) and Urine hCG +ve. USS abdomen free fluid + with no Intra-uterine pregnancy.

At peripheral hospital an emergency mini laparotomy was performed.

Findings: No tubal pregnancy; No haemo-peritoneum; Free-fluid in the abdomen 200ml.

Preoperative investigations were received after the surgery: Hb 10.5g/dL, PLT $82 \times 10^9/L$

Treatment given post operatively: 02 Units PRC, 01 Unit Voluven, 03 Units Normal Saline. Patient was transferred to ICU for further management.

Referral Hospital ICU Assessment and Care: No fever, conscious & rational (GCS 15/15). Not pale, mildly icteric, CRFT <2 secs. BP 115/75 mmHg. HR 110/min. Lungs B/L reduced air entry. Abdomen soft but oozing from surgical site.

Investigations: WBC 6,800 cells/L; PLT $39 \times 10^9/L$; INR 1.53; Dengue NS1 (-) ve, IgM/IgG (+) ve.

USS B/L pleural effusion and moderate ascites.

Two hours later: Increased oozing from surgical site. BP 88/67mmHg; PLT $39 \times 10^9/L$, PCV 32%

Treatment: IV Hartmann's boluses given, IV Antibiotics started.

Next day: in spite of fluid therapy, with inotropes BP did not pick up and patient developed respiratory distress with dyspnoea and tachypnoea (RR 36/min). Despite ventilatory support patient expired on the same day.

Pitfalls:

1. Did not consider history of fever especially when afebrile on presentation.
2. When presenting in shock ignoring Dengue Shock Syndrome (DSS) as a differential diagnosis.
3. Not considering warning signs of leaking – faintishness, abdominal pain (signs of impending shock)
4. Little attempt to resuscitate the state of shock; must perform an urgent FBC and interpret before emergency surgical intervention.
5. Patient presenting in shock with free fluid in abdomen (also seen on initial USS) indicates that the patient has already leaked for a significant period of time. With PLT count $< 50 \times 10^9/L$ this patient was probably in the latter part of the critical phase. Therefore, indiscriminate use of IV fluids (crystalloids) had led to fluid overload.
6. In patient presenting with hypotensive shock (decompensated) should consider leaking and bleeding (PCV 32%) both, with acidosis, hypocalcaemia, hypoglycemia and early organ involvement.
7. In a DSS patient with a low PCV of 32% should consider significant bleed requiring early blood transfusions (rapidly) until patient becomes haemodynamically stable.
8. Important to exclude DHF/DSS when considering surgical intervention for appendicitis, renal colic, etc. with history of fever and abdominal pain.

10.2 CASE - #2

A 28 year old primi para, at POA 32 weeks, admitted to the casualty ward of a maternity hospital one morning around 9.00am. Presenting complaint was upper abdominal pain and reduced foetal movements of one days duration.

O/E: BP 150/100mmHg. Albuminuria 1+. Although there was no history of preeclampsia, HELLP syndrome was suspected. FBC and liver function tests were ordered. USS abdomen revealed normal foetal heart beat and foetal movements.

She was treated with Nifedipine 10mg SR and her BP dropped to 90/50 mmHg. Her HR remained around 100 beats per minute. With a NS bolus of 250 ml given over 30 mins. her BP picked up to normal. She was on a NS slow drip thereafter. Medical opinion sought and clinical diagnosis of HELLP syndrome was established.

That evening around 3.30pm, morning FBC results revealed Platelet count of $9 \times 10^9/L$. Attending Obstetrician thought the counts were too low to be due to HELLP. On further inquiry it was revealed that the patient has had a history of fever for 4 days and afebrile for 48 hrs prior to admission. At that point blood was drawn for dengue Ag and IgM, IgG and the patient was moved to ICU for further management.

She was taken to ICU (6.30pm same day): conscious rational, RR 38, SpO₂ 100%, bilateral air entry reduced in lungs R>L, HR 89, BP 123/86, CRFT 5s, abdomen was distended & tender, UOP 70ml/6 hrs (approx. 12 ml/hr), Platelets 9×10^9 , WBC 13,000 (N-82%, L-14%, Hb-15.9%, HCT 48.7%), ALT 147, AST 468, CRP 41.6, Dengue Ag +ve (at 11pm), VBG pH 7.16, PCO₂ 35, PO₂ 35, BE -21 mmol/l.

Expert medical opinion sought for further management revealed patient having DHF in latter part of leaking with fluid overload, liver dysfunction and acidosis.

Following day early morning patient became dyspnoeic, abdominal distension increased and UOP reduced further. Patient was intubated and ventilated while CRRT was also considered.

Pitfalls:

1. At first contact fever history was not elicited which led to deviation from diagnosing dengue.
2. Measuring of BP technique was not documented – in pregnancy left later position is ideal (to get proper values).
3. Warning feature of impending shock of DHF such as abdominal pain was not evaluated.
4. Tachycardia (HR 100) without fever should have been interpreted and acted upon. Immediate A, B, C, S assessment and consider blood transfusion.
5. FBC done in the morning was available and read that evening – FBC is an urgent investigation and should be ideally read within one hour of blood collection.

6. Clinical detection of fluid with B/L pleural effusion with a low platelet count of $9 \times 10^9/L$ is seen in latter part of leaking in DHF where major part of leaking is over.
7. More fluid given at late stage of leaking led to fluid overload and respiratory distress requiring ventilatory support.
8. In this patient acute liver and renal dysfunction with acidosis was probably due to suboptimal fluid therapy during early critical phase.

10.3 CASE - #3

A 32-year old previously healthy P₂C₁ woman in her 36th week of POA in early labour, indication being past section, was brought for caesarian section to OT. Attending anesthetist noted a low platelet count of $76 \times 10^9/L$ With WBC 7,200 cells/L, HCT 36%.

On further inquiry she has had fever for 3 days before admission to hospital. Urgent NS1 Ag test was found positive. USS abdomen and chest showed no free fluid. On suspicion that the patient may go into critical phase soon the multidisciplinary team discussed and decided to postpone the delivery although a concern on possible uterine rupture was noted. Patient was admitted to ICU and closely monitored for both fluid leakage due to DHF and uterine rupture. It was noted that the uterine contractions ceased without any tocolytics. However, patient developed plasma leakage about 6 hrs later. Her platelet dropped to $30 \times 10^9/L$ and she developed R/S pleural effusion although her HCT remained within 34-40%. She was managed with fluids according to the guidelines. Continuous CTG was done to detect any foetal compromise.

Her HR and BP remained within normal ranges throughout the critical phase. Her UOP was adequate. Liver enzymes were between 100-200/IU/L AST >ALT.

Around 56 hrs she was on recovery phase with platelet count of $75 \times 10^9/L$, WBC 30,000 cells/ μL with neutrophil leukocytosis and CRP 118. She also developed itching of palms and soles. She had no fever and was haemodynamically stable. ROTEM testing for coagulation remained within normal ranges. Suspecting sepsis, broad-spectrum antibiotics were started. Foetal condition remained normal.

At this stage a decision was made to deliver the foetus by caesarian section under spinal anesthesia. During surgery there was no blood and pus noted in the peritoneal cavity. Live baby was delivered. She made an uneventful recovery and both mother and baby were discharged 4 days after surgery.

Pitfalls:

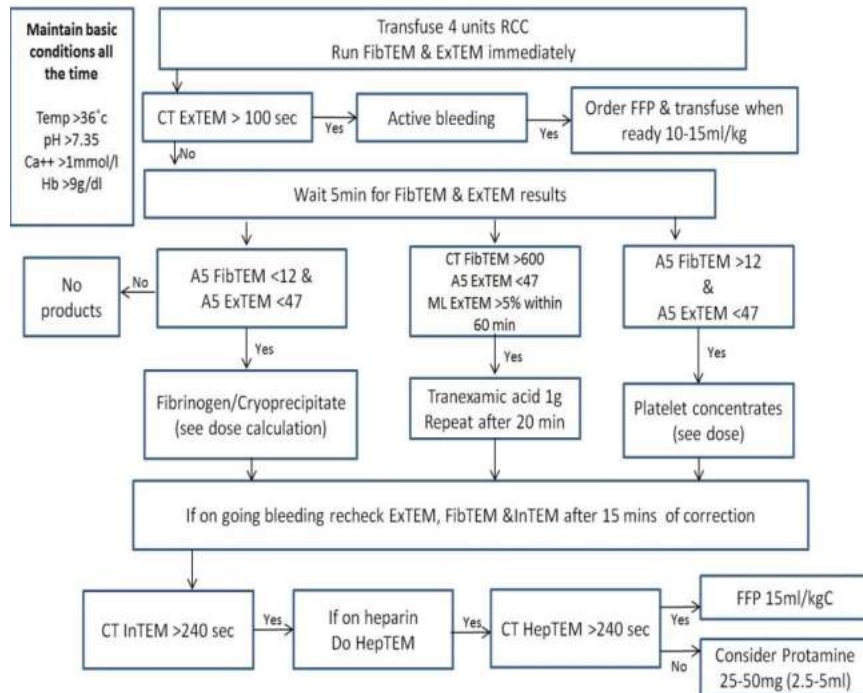
1. History of fever was elicited late and FBC was considered just before surgery
2. Not considering close observation of baby after delivery for vertical transmission of dengue virus.

Annexure 3

MANAGEMENT OF MASSIVE OBSTETRIC HAEMORRHAGE

Blood loss >40% of blood volume (Blood volume calculated as 100ml/kg)

Guided by results from ROTEM-CSHW



Fibrinogen/Cryoprecipitate dose

Target increase in A5 FibTEM (mm)	Fibrinogen mg/kg BW	Cryoprecipitate (ml/kg)/ units
2	12.5	1ml/kg(5u)
4	25	2ml/kg(10u)
6	37.5	3ml/kg(15u)
8	50	4ml/kg(20u)
10	62.5	5ml/kg(25u)
12	75	6ml/kg(30u)

Platelet dose

A5 ExTEM	Dose
<35mm	4 units platelets
<25mm	8 units platelets
<15mm	8 units platelets + Cryo

Ref: Dr. Klaus Görlinger A5 Algorithm and LWH UK Protocol

Annexure 4

COMMON HAEMATOLOGICAL PARAMETERS DURING PREGNANCY

Parameter	Range of normal values			
	Non-pregnant	Trimester 1	Trimester 2	Trimester 3
Hemoglobin (g/dL)	12.0 – 15.8	11.0 -13.9	10.6 – 14.8	9.5 – 15.0
Hematocrit (%)	35.4 – 44.4	33.0 – 41.0	32.0 – 39.0	30.0 – 40.0
WBC	3.5 – 9.1	5.7 – 13.6	5.6 – 14.8	5.9 – 16.9
APTT (s)	26.3 – 39.4	23.0 – 38.9	22.9 – 38.1	22.6 – 35.0
AST (SGOT) IU/L	10- 40	4 - 40	10 - 33	4 - 32
ALT (SGPT) IU/L	7 – 41	1 - 32	2 - 34	2 - 32


Source: Bauer KA et al, Maternal adaptations to pregnancy: Hematologic changes

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