NATIONAL GUIDELINE FOR CLINICAL MANAGEMENT OF DENGUE

5th Edition 2025

National Malaria Elimination & Aedes Transmitted Disease Control Programme,CDC,DGHS,Mohakhali,Dhaka

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Contents:

Messages from Director General of Health Services

Dengue was fairly unfamiliar disease in Bangladesh when first outbreak occurred in 2000. The enormous morbidity and unacceptable mortality during early years were taken care with great emphasis and importance by early response and management of cases. The Communicable Disease Control Division of Directorate General of Health Services felt the necessity of developing national guideline in 2000 for the clinical management of dengue by customizing the SEARO/WHO guidelines in accordance with the prevailing local situation for providing appropriate management for dengue patients to mitigate the morbidity, prevent regrettable mortality and raise awareness for appropriate prevention and control in community.

The third edition of the 'National Guidelines for Clinical Management of Dengue Syndrome was developed in 2013 which was updated in 2018 (4th edition) based on the version of WHO/SEARO guideline by the participation of physicians, pediatricians, national controlprogram personnel and researchers as a tool to provide a uniform, scientific, affordable and appropriate clinical management as well as to eradicate prevailing confusions and ambiguity.

A significant surge began in 2019 and remained notably evident in the years 2021, 2022, 2023 and 2024. In 2019, over one hundred thousand cases were reported, along with nearly two hundred deaths. The biggest ever outbreak occurred in 2023, with a total of 321,179 laboratory confirmed dengue cases and 1,705 deaths, one-third of which were reported from Dhaka city. The disease also spread throughout the country. The presentation of the disease with different serotypes was non-identical to previous years as well. So, Communicable Disease Control Programme felt the necessity of publishing a revised and expanded edition of the existing guideline with some updates and modifications.

I would like to thank everyone, who contributed to this guideline. It will surely serve to the need of the physicians at all levels in clinical management of Dengue. Together, we will march forward to create a healthy Bangladesh.

Prof. Dr. Md. Abu Jafor
Director General
Directorate General of Health Services

Preface

Dengue is an important tropical infection caused by an Arbo-virus named 'Dengue virus'. As a mosquito borne disease it is widely spread in many tropical countries favorable for transmission. Millions of world populations are affected by this viral infection. Each year, thousands of dengue infections are reported and there are several upsurge of dengue in many countries includinwg Bangladesh.

Fighting with dengue upsurge is important in public health. Usually, patients of dengue present the classical symptoms, acute febrile illness with or without haemorrhagic manifestation. However, in recent days some cases of dengue presented atypical clinical presentations made the diagnosis and management procedures complicated.

The severity of infection as well as the mortality vary depending on different factors. The medical facilities and skill of attending physicians are important determinants in the outcomes of dengue case management. All these highlight the needs of the updated knowledge on clinical management of dengue illness. I hope this updated version of the guideline will be very helpful to effective management of dengue.

I extend my gratitude to the expert group for their valuable contribution in updating this guideline. I am also thankful to those who contributed at different sections of the finalization of this document including WHO and other development partners. Constructive advice from the users and multiple stakeholders will help to update the guideline in future.

I wish the best utilization of this guideline.

Prof. Dr. Md. Halimur Rashid
Line Director, Communicable Disease Control
Directorate General of Health Services

Message from Editorial Board

Dengue fever is closely known to us for about 2 decades. The impact of illness due to Dengue on our health care system has made it very familiar in our society. The disease is very much related to our environment, economy and national policy. The need for publishing this fifth edition is very rational in the context of national and global demand. Updating the knowledge on clinical management of dengue illness is very essential. The first edition published in 2000, 2nd edition in 2009, 3rd edition in 2013 and fourth edition in 2018.

The Communicable Disease Control Division of DGHS, Ministry of Health and Family welfare in collaboration with World Health Organization country office conducted series of meetings, group discussion and presentation by a talented group of Physicians, Pediatricians, Microbiologist, Gynecologists and Entomologists for updating this edition of national guideline. I express my heartfelt thanks and gratitude to the authorities that they entrusted on us. I am also thankful to the specialists who have contributed a lot for making the fifth edition a successful one.

This guideline is intended to reach all level of the health care services which could lead to reduce morbidity and mortality due to dengue illness. The fifth edition 2025) contains new conception regarding pediatric management as well as management of Dengue in pregnancy and children, which will help with the aim of early diagnosis and effective management of Dengue of all groups of population. Due to the change in disease pattern of Dengue, some modifications were needed to be included to this existing edition.

I extend my gratitude to each and every one who contributed towards the development of this guideline.

Acknowledgement of Communicable Disease Control

National Malaria Elimination & Aedes Transmitted Diseases Control Program (NME & ATDCP) under the leadership of Communicable Disease Control Division, DGHS is playing strategic stewardship and governance roles in combating the deadly diseases like dengue and malaria in Bangladesh. National program deemed it as utmost priority to update the existing National Guideline for Clinical Management of Dengue (Fifth edition 2025) and included paediatric management as well as management of Dengue in pregnancy and children in the updated version.

Here we gratefully acknowledge the contributions of Physicians, Paediatricians, Gynaecologist and Epidemiologists working in various reputed institutes of Bangladesh, WHO Bangladesh and program personnel for finalizing this document through various consultative meetings and workshops. We extend our heartiest congratulations to all of them for their hard work in bringing out this updated guideline to light. We are grateful to the Ministry of Health and Family Welfare and DGHS for continuous guidance in preparation and finalization of this document.

Abbreviation and acronym

ADE	Antibody dependent enhancement	ALT	Alanine aminotransferase
AMTSL	Active Management of the Third Stage of Labor	AST	Aspartate aminotransferase
AFI	Amniotic fluid index	APH	Antepartum Haemorrhage
ABG	Arterial blood gas		
BMI	Basal metabolic index	CRFT	Capillary refill time
CFR	Case fatality rate	CTG	Cardiotocography
DENV	Dengue virus	DSS	Dengue shock syndrome
DHF	Dengue haemorrhagic fever	DAPT	Dual antiplatelet drug
DIC	Disseminated intravascular coagulation	EBQI	Evidence-Based Quality Improvement
EBP	Evidence based practice	EDS	Expanded dengue syndrome
FHR	Fetal heart rate	Hct	Haematocrit
GDM	Gestational diabetes mellitus.	HLS	Hemophagocytic lymphohistiocytosis
HELLP	Hemolysis, elevated liver enzyme and low platelet	ICP	Intracranial pressure
IMCT	Integrated Management of Childhood Illness	LMWH	Low molecular weight heparin
LSCS	Lower segment cesarian section	MHD	Maintenance hemodialysis
MICU	Medical intensive care unit	MOF	Multiorgan failure
NICU	Neonatal intensive care unit	NLR	Neutrophil to lymphocyte ratio
NS1	Nonstructural protein 1	OPD	Outpatient department
MOF	Multiorgan failure	PCV	Packed cell volume
PT	Prothrombin time	PCF	Pericholecystic fluid
PRC	Packed red cell	POCUS	
PPH	Post partum haemorrhage	PIH	Pregnancy-induced hypertension
TT	Thrombin time	UHFWC	Union health and family welfare center
PCO2	Partial pressure of carbon dioxide	UHTC	Urban **health** training center
VBG	Venous blood gas	VKA	Vitamin K antagonist

Level of evidence

Level of Evidence	Description
Level 1	Evidence from a systematic review or meta-analysis of all relevant RCTs (randomized controlled trials).
Level 2	Evidence from at least one well-designed RCT (e.g. large multi-site RCT).
Level 3	Evidence from a single well-designed controlled trial without randomization (aka quasi-experimental studies) OR a systematic review of a complete BOE (integrative review of higher and lower evidence) OR mixed methods intervention studies
Level 4	Evidence from well-designed case-control or cohort studies
Level 5	Evidence from systematic reviews of descriptive and qualitative studies (meta-synthesis)
Level 6	Evidence from a single descriptive or qualitative study, EBP, EBQI and QI projects
Level 7	Evidence from the opinion of authorities and/or reports of expert committees, reports from committees of experts and narrative and literature reviews

*Adapted from: Melnyk, & Fineout-Overholt, E. (2023). *Evidence-based practice in nursing & healthcare: A guide to best practice* (Fifth edition.). Wolters Kluwer.

This dengue guideline was tried to prepare based on evidence but all its information not thoroughly followed the level of evidence.

Aims of this guideline

- Understanding Dengue in a comprehensive way and offers best clinical advice.
- Diagnosis and management at all tiers of care, community to hospital through a triage system.
- Uniform use of available tools in a systematic manner customized to local situation.

To whom this guideline is intended

- Clinicians who are in direct care of Dengue patients.
- Programme personnel who are involved for prevention and control of Dengue.
- Health Care Managers and Policy Makers and Hospital Managers responsible for the planning and implementing various plans, operations, programs and activities.
- Medical Students and Residents for customizing the working knowledge.

Dengue in Adult

Chapter-1

1.1 Introduction

Dengue is a disease caused by an arbovirus, which has four serotypes and that is transmitted by Aedes aegypti and Ades albopictus mosquito. It is regarded as the most important arthropod transmitted human viral disease, and constitutes an important global health problem. Dengue ranks as the most important, rapidly emerged disease in recent years and is endemic in all continents. It has shown an increase due to various reasons-construction activities, lifestyle changes, deficient water management, improper water storage, stagnation of rain water in containers lying outside houses and practices leading to proliferation of vector breeding sites in urban, semi-urban and rural areas.

Dengue virus infections may be asymptomatic or may lead to undifferentiated fever, dengue fever, or dengue haemorrhage fever (DHF) with plasma leakage that may lead to Dengue Shock Syndrome (DSS). This range of manifestations of dengue virus infection may be defined as Dengue Syndrome

1.2 Epidemiology

The epidemiological triad, a model used to understand the factors contributing to disease spread, consists of three components:

- Agent (eg. dengue virus)
- Host (e.g. humans), and
- Environment (external factors that facilitate disease transmission such as rainfall, temperature, humidity)

The epidemiology of dengue is conventionally linked to environmental factors of the triad, and further complicated by anthropological elements, including cultural, behavioral, and habitation factors. Its transmission remains low due to extreme of temperature with low relative humidity and absence of mentioned anthropological risk factors. Temperatures in the range of 25°C ± 5°C, relative humidity around 80% and innumerable small water collections result high transmission.

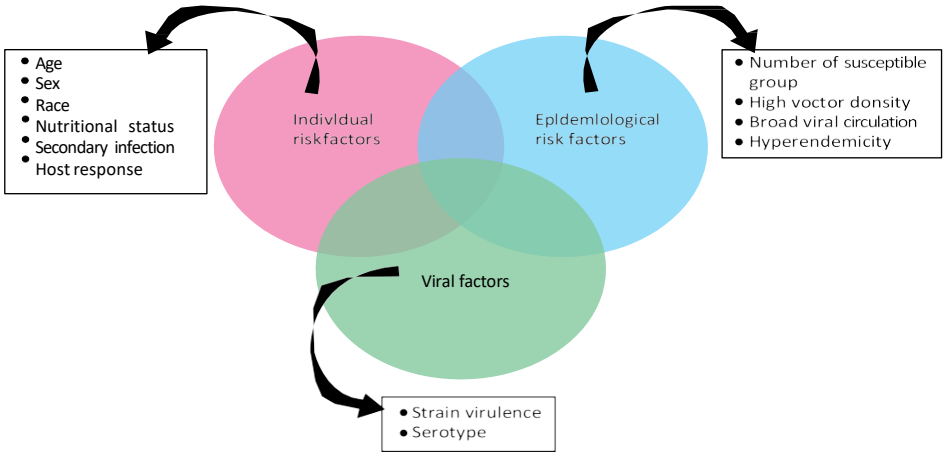


Figure 1: Risk factor for dengue haemorrhagic fever. (Hadinegoro, Revised WHO dengue classification 199734 Paediatrics and International Child Health 2012)

Dengue, once a seasonal disease in Bangladesh confined mostly to urban areas, has evolved into a year-round concern, with cases now reported nationwide. The seasonal pattern has also changed, with cases usually peaking in the third quarter and, in some years, extending into the final quarter

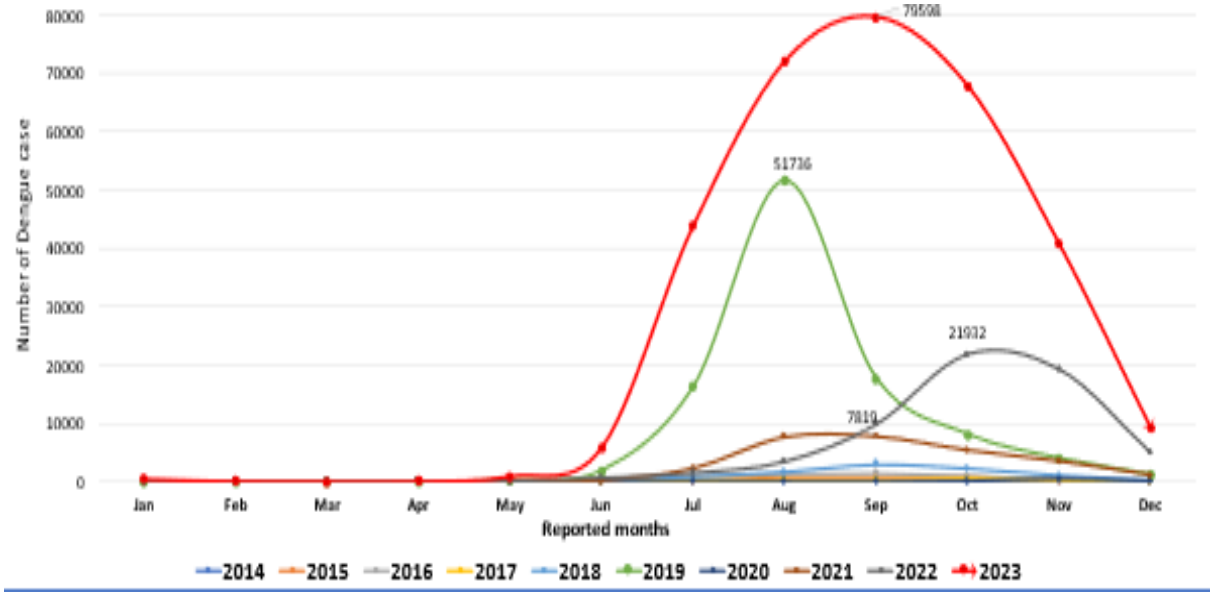


Figure 2: Seasonal variation of dengue (DGHS, MIS and WHO Country office, Bangladesh)

The provided chart illustrates the number of reported dengue cases in Bangladesh from 2014 to 2023, highlighting the seasonal trends and yearly variations.

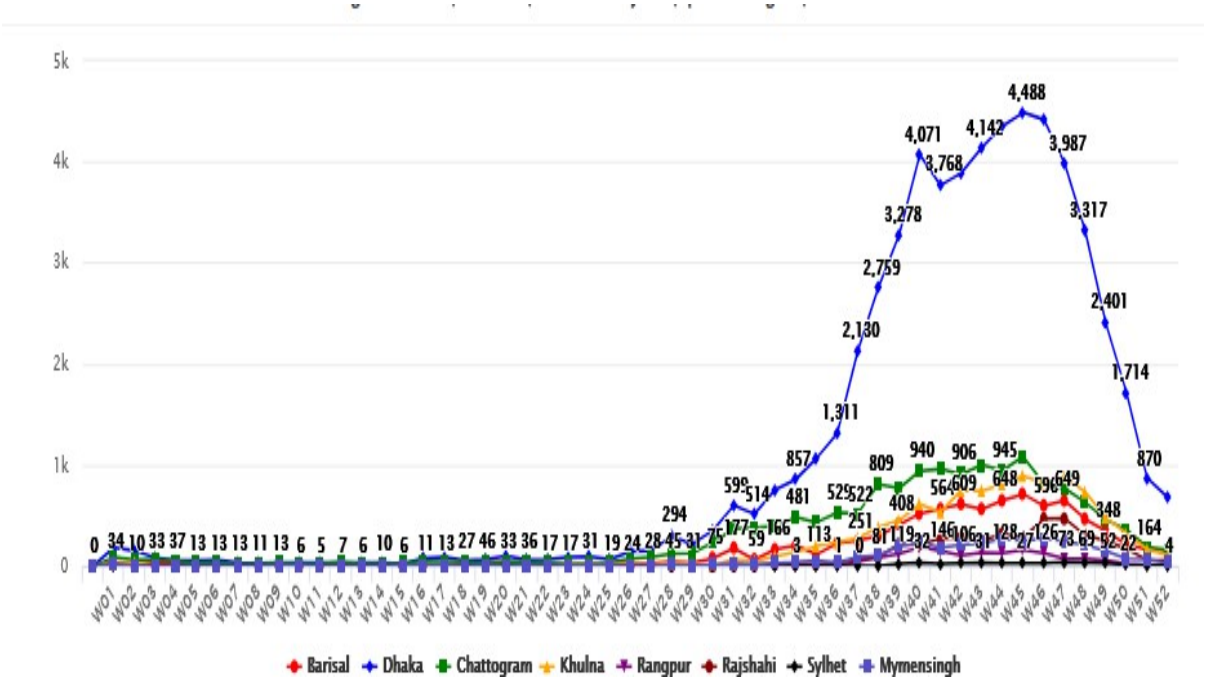


Figure 3: Dengue affected (Admitted) in division by EPI (Epidemiological) Week in 2024, Bangladesh. (Health Emergency Operation Center & Control Room, Bangladesh)

1.2.1 Dengue Virus:

The dengue virus forms a distinct complex under the genus flaviviruses based on antigenic and biological characteristics. There are four dengue virus serotypes which are designated as DENV-1, DENV-2, DENV-3, and DENV-4.

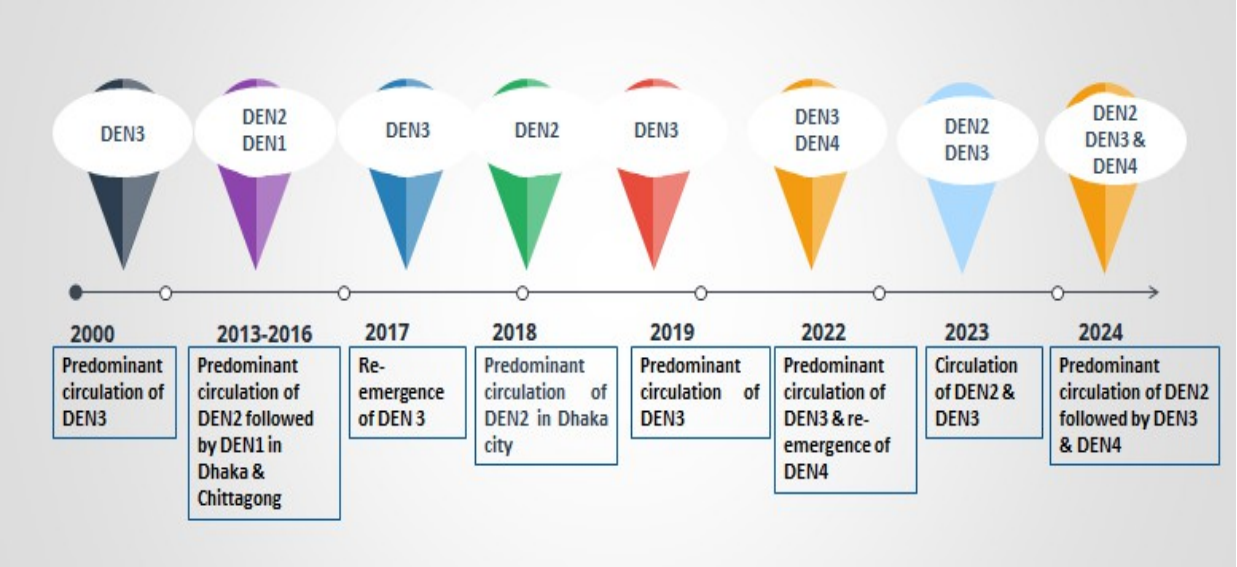


Figure 4: Dengue serotype by years. (DGHS, MIS and WHO Country office, Bangladesh)

The image depicts the temporal distribution of dengue virus serotypes in Bangladesh from 2000 to 2024. It shows the predominant circulating serotypes of the dengue virus (DENV) in different years from the early 2000s, DEN-3 was the predominant serotype circulating in Bangladesh, and it notably re-emerged in 2017. Between 2013 and 2016, DEN-2 became prevalent, followed by DEN-1, particularly in Dhaka and Chittagong. In 2018, DEN-2 was the dominant strain in Dhaka city. By 2019, DEN-3 had once again become the predominant serotype. In 2022, DEN-3 maintained its dominance, with DEN-4 re-emerging as a significant serotype. In 2023, both DEN-2 and DEN-3 were the primary strains circulating in the country. Den 2 continued as the predominant serotype (70%) in 2024 followed by Den 3 (20%) and Den 4 (9%).

Although all four serotypes are antigenically similar yet they elicit cross protection for only few months. Secondary infection with dengue serotype 2 or multiple infection with different serotypes enhance chances of occurring more severe form of diseases.

1.2.2 Dengue Vector:

Dengue is primarily transmitted by mosquitoes, with ***Aedes aegypti*** being the main vector, and ***Aedes albopictus*** playing a secondary role in some regions. These mosquitoes are most active during the day, especially in the early morning and late afternoon.

Aedes aegypti is highly domesticated and strongly anthropophilic. It needs more than one bite to complete one blood meal and needs more than one blood meal to complete one gonotrophic cycle. These habits result in the generation of multiple cases and clustering of dengue cases in the cities.

Aedes aegypti primarily breeds in urban environment, where stagnant water can accumulate in artificial containers such as flowerpots, discarded plastic containers, usually found in close proximity to human dwellings.

Aedes albopictus, may found in natural water sources such as tree holes, bamboo stumps, plant axils. This species is more likely to thrive in rural and sub-urban environments as well as forested areas. It is an aggressive feeder and can take the amount of blood they need for each gonotrophic cycle in one bite.

1.3 Transmission Cycle:

The female mosquito usually becomes infected with the dengue virus when it takes a blood meal from a person during the acute febrile (viraemia) phase of dengue illness. After an extrinsic incubation period of 8 to 10 days, the mosquito becomes infected. There is also evidence of vertical transmission of dengue virus from infected female mosquitoes to the next generation. The virus is transmitted when the infected female mosquito bites and injects saliva into the person bitten. Dengue begins after an intrinsic incubation period of 4 to 7 days (range 3–14 days).

There is evidence however, of the possibility of maternal transmission (from a pregnant mother to her baby). Rare cases of transmission via blood products, organ donation and transfusions have been recorded

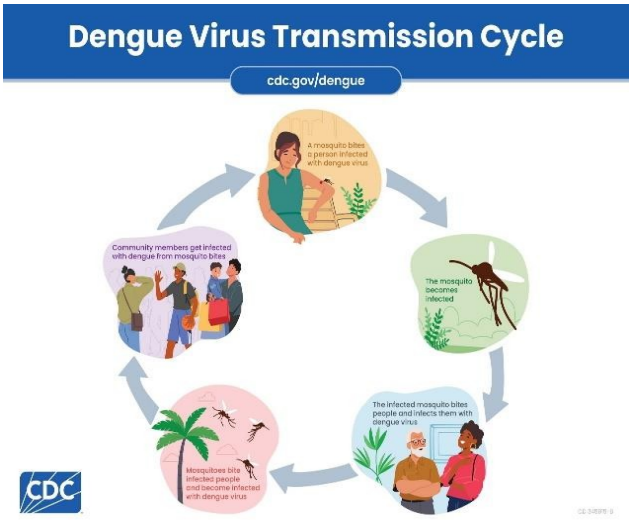


Figure 5: Dengue transmission cycle cdc.gov/dengue

A mosquito bites a person infected with dengue virus. The mosquito becomes infected. The infected mosquito bites people and infects them with dengue virus. Mosquitoes bite infected people and become infected with dengue virus. Community members get infected with dengue from mosquito bites.

1.4 Global Burden of Disease:

Before 1970, only nine countries had experienced severe dengue epidemics. The silent expansion of vectors has played a significant role in spreading dengue to over 130 countries, putting nearly 4 billion people at risk. From 2010 to 2023, dengue cases surged from 2,430,203 to 6,590,872, and deaths rose from 4,271 to 7,400. By April 2024, 7,308,219 cases and 3,720 deaths were reported from 89 countries to WHO, indicating a critical situation. This, beside engaging Whole of Government and Whole of Society in vector control and service delivery, necessitates integrated surveillance, community empowerment, effective communication, and research.

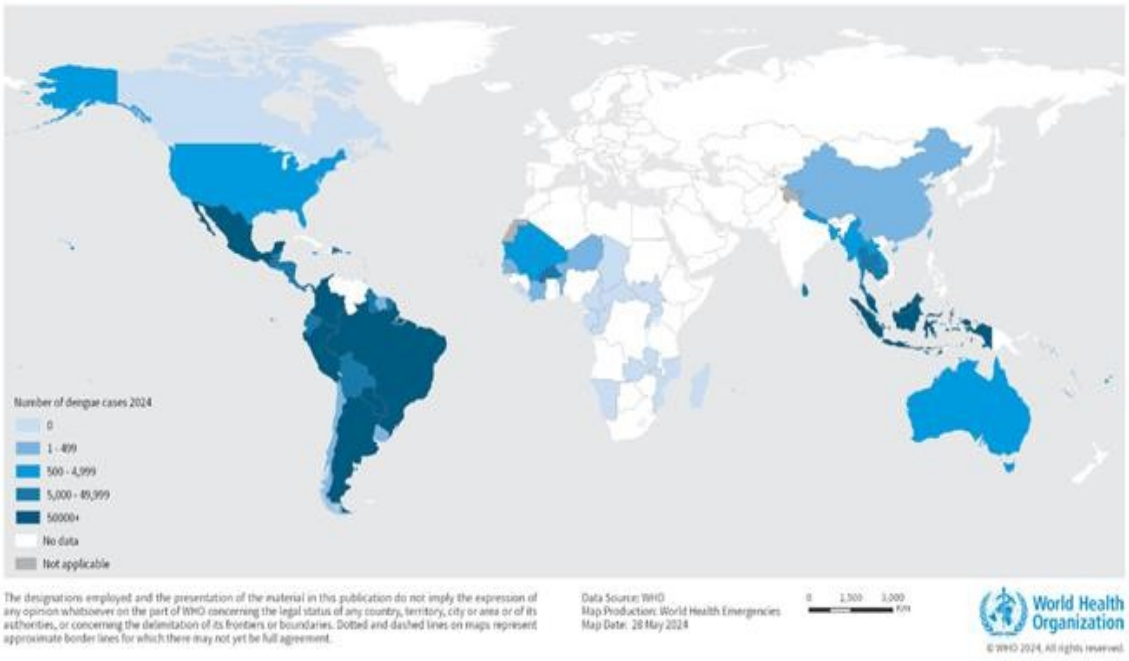


Figure 6: Geographical distribution of dengue cases as reported to WHO from January to April 2024

1.5 Dengue Burden in Bangladesh:

Dengue was first recorded in Bangladesh in the early 1960s and was known as “Dacca fever". Since then, it is marked by periodic outbreaks and increasing prevalence over the years.

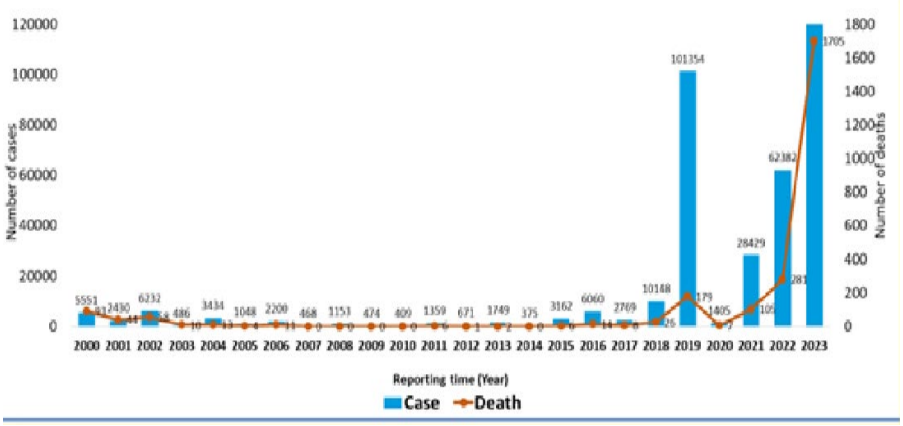


Figure 7: Dengue cases and deaths with periodic outbreak by times: year 2000 to 2023 Source: ACAPS using data from Hossain et al. (11/07/2023); DGHS (17/09/2023)

A significant surge began in 2019 and remained notably evident in the years 2021, 2022, 2023 and 2024. In 2019, over one hundred thousand cases were reported, along with nearly two hundred deaths. The biggest ever outbreak occurred in 2023, with a total of 321,179 laboratory confirmed dengue cases and 1,705 deaths, one-third of which were reported from Dhaka city. In 2024, total number of admitted dengue case were 101214 and total deaths were 575.

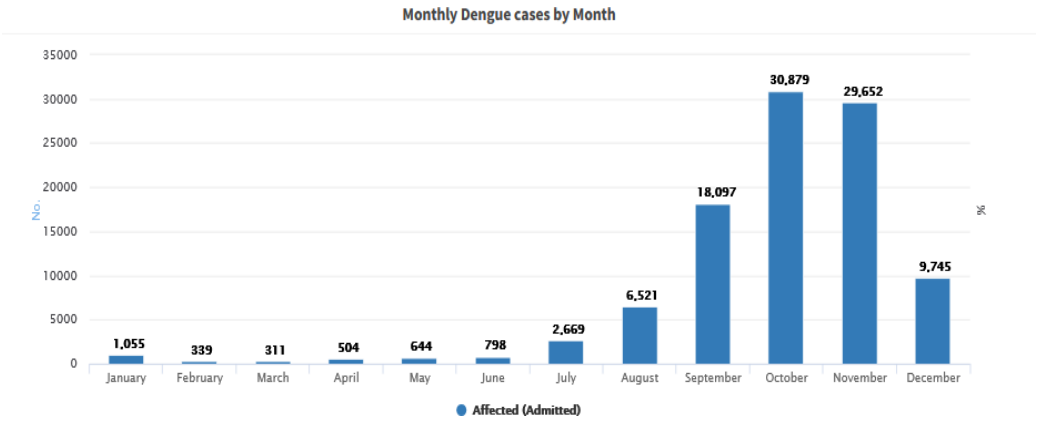


Figure 8: Monthly trend of dengue cases in 2024. (Health Emergency Operation Center & Control Room, Bangladesh)

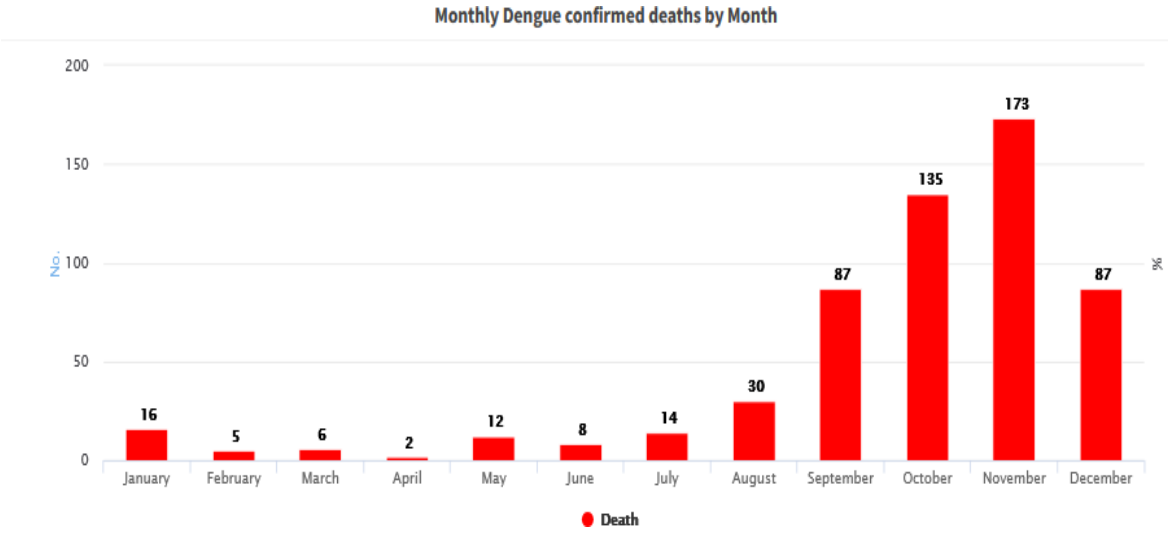


Figure 9: Monthly trend of dengue death in 2024. (Health Emergency Operation Center & Control Room, Bangladesh)

With over 90% of dengue infections being asymptomatic, their potential role in silent transmission has attracted considerable attention in both epidemic and non-epidemic settings. Another study highlights that up to 80% of all dengue infections are asymptomatic, with less than 5% of cases progressing to severe forms, and only a small fraction resulting in fatalities. These cases are usually unreported, remain in the community and contributing to further transmission through mosquitoes and exacerbating the ongoing rise in dengue cases.

Dengue, particularly since 2023, has become a year-round concern nationwide, whereas it was previously seasonal and primarily confined to urban areas.

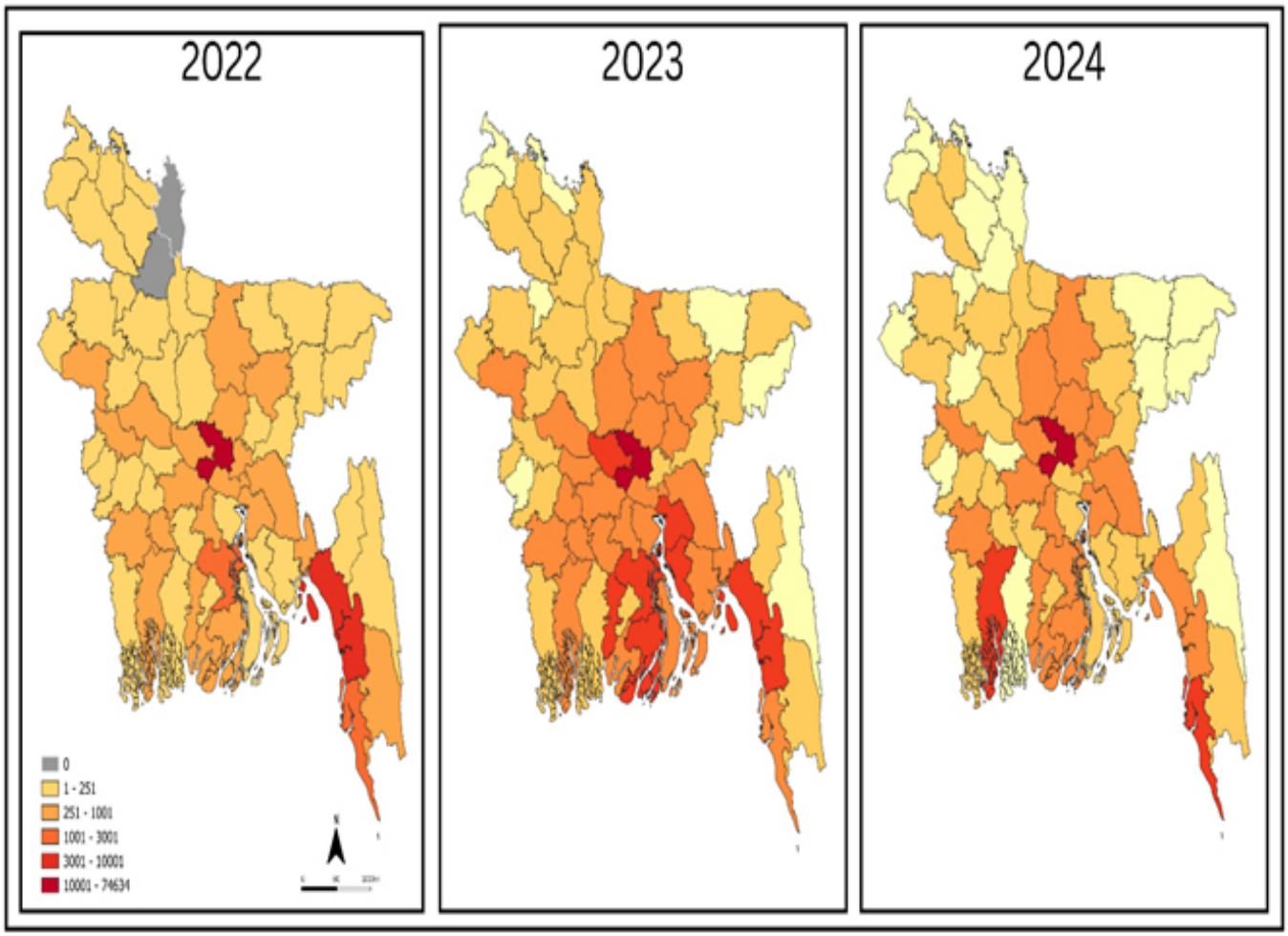


Figure 10: Dengue cases by districts in Jan-Dec 2021, 2022 and 2023 (DGHS, MIS and WHO Country office, Bangladesh) Figure depicts spread of dengue gradually over the years.

1.5.1 Dengue mortality in Bangladesh:

The dengue case fatality rate (CFR) in Bangladesh has risen from 0.26% in 2018 to 0.53% in 2023, one of the highest in the world. About 74% of these deaths were due to Dengue Shock Syndrome (DSS), with 81% occurring within three days of hospitalization. The peak in cases and deaths was observed in September 2023 with 79,598 cases and 396 deaths.

Chapter-2

2.1 Pathophysiology of Dengue Infection

Infection with one serotype confers life-long immunity to that serotype and cross-immunity to other serotypes for 2-3 months only. However, secondary infection with another serotype or multiple infections with different serotypes leads to severe dengue.

The pathogenesis of dengue involves a complex interaction between virus and host factors and remains incompletely understood. The immune system plays a key role in disease pathogenesis. Various mechanisms of severe disease have been suggested, including:

- Antibody-dependent enhancement (ADE)
- T-cell mediated release of inflammatory cytokines in heterotypic re-infection
- Complement activation by virus-antibody complexes
- Cytokine storm
- Vasculopathy
- Coagulopathy

2.1.1 Antibody-dependent enhancement:

Dengue infection produces two types of antibodies**:** neutralizing and non-neutralizing. Non-neutralizing cross-reactive antibodies elicited in a primary infection bind virus in a secondary infection and then have a greater ability to infect Fc-receptor-bearing cells (monocytes, macrophages). This is called ADE and potentially leads to an increased viral biomass, and therefore more chance of developing severe disease.

2.1.2 T-cell mediated killing of dengue virus in heterotypic re-infection:

Upon termination of primary infection, memory DENV–specific T cells are formed and are retained with a higher frequency compared to other naïve cells. This immune response could last a lifetime. In a secondary infection with the different serotype of DENV infection heterotypic infection), the virus will induce a memory response that activates highly specific T-cell responses and leads to increased release of inflammatory cytokines.

2.1.3 Complement activation by virus-antibody complexes:

DENV NS1 is implicated in disrupting endothelial monolayer by activating immune cells through Toll-like Receptor 4 (TLR 4) and activating complement cascade.

2.1.4 Cytokine storm:

CD4+ and CD8+ T cells, specific to the dengue virus, cause lysis of virus-infected cells and produce cytokines such as IFN-gamma, Tumour Necrosis Factor (TNF)-alpha, and lymphotoxin. These cytokines result in a “cytokine storm” and ultimately lead to severe disease. Moreover, IFN-gamma also enhances the expression of immunoglobulin receptors, which augments the antibody-dependent enhancement of infection. Therefore, this disproportionally enhanced immune response, particularly in secondary heterologous infections, is responsible for various pathogenetic mechanisms such as vasculopathy, coagulopathy, and organ involvement.

2.1.5 Vasculopathy:

Initially, there occurs a transient disturbance in the function of the endothelial glycocalyx, which leads to a temporary alteration in the characteristics of the fiber matrix of the endothelium. Anti-NS1 antibody acts as autoantibodies and cross-react with platelets and non-infected endothelial cells, which triggers intracellular signaling and disturbances in capillary permeability. Plasma leakage occurs due to capillary permeability and manifests as a combination of haemoconcentration, pleural effusion, pericardial effusion, ascites, and multi-organ dysfunction.

2.1.6 Coagulopathy:

The causes of coagulopathy in dengue fever are multifactorial, and the underlying mechanism remains unclear. Primarily, relatively consistent findings are an increase in an activated Partial Thromboplastin Time (aPTT) and reduced fibrinogen concentrations. Thrombocytopenia associated with coagulopathy increases the severity of bleeding. The release of heparan sulfate or chondroitin sulfate from the glycocalyx also leads to coagulopathy. Moreover, disseminated intravascular coagulation (DIC) also leads to coagulopathy.

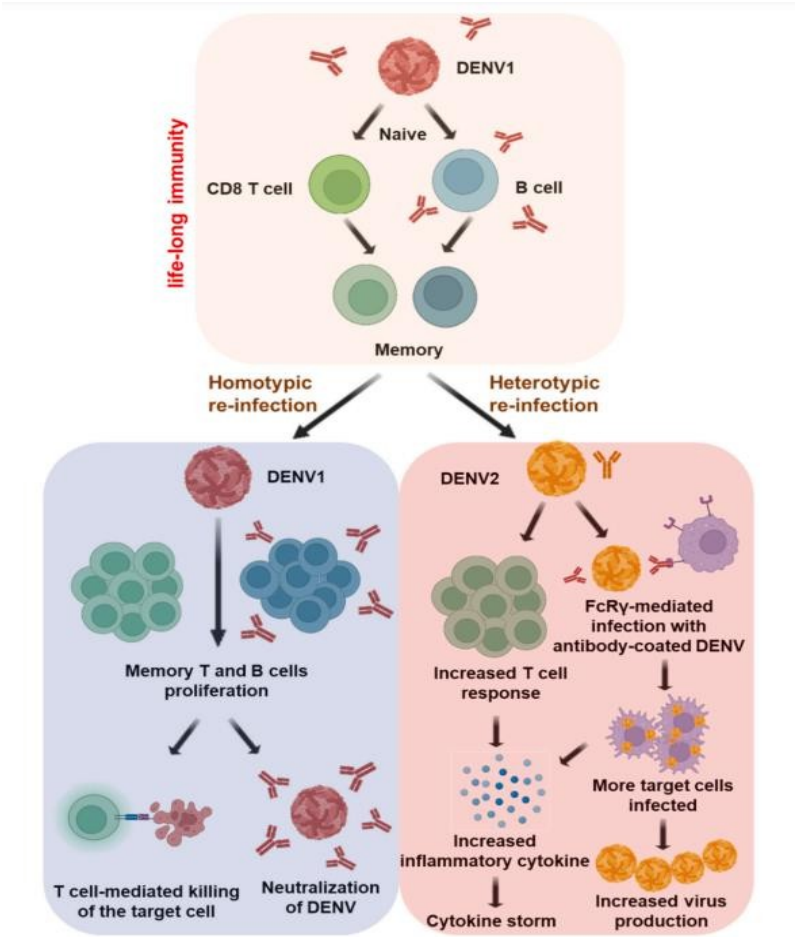


Figure 11: Primary and secondary homotypic and heterotypic DENV infection.
Source: Khan, M. B. et.al (2023). Dengue overview: An updated systemic review. Journal of Infection and Public Health.

Ultimately heterotypic dengue infection causes ADE, cytokine storm and complement activation that leads to Vasculopathy → Capillary leakage→ Shock (level 1).

- Coagulopathy → severe bleeding
- Cytopathy → Leucopenia and thrombocytopenia
- Organopathy → Multiorgan failure

2.2 Causes of bleeding in Dengue Syndrome:

- Abnormal coagulation
- Thrombocytopenia
- Platelet dysfunction
- Prothrombin complex deficiency secondary to liver involvement
- Endothelial injury
- DIC

2.3 Factors Responsible for DHF/DSS:

- Re-infection: Heterotypic re-infection or multiple infections with different serotypes leads to severe form of dengue
- Serotype: DENV-2 is an associated factor for DSS

Chapter-3

3.1 Classification and clinical manifestations of Dengue

The natural course of the illness:

The clinical manifestation of dengue infection varies according to the virus strain and host factors such as age, immune status, etc. Many patients infected with dengue virus remain asymptomatic. Symptoms develop after an incubation period of 4-7 days (range 3-14 days) and symptomatic patients may have one of the following conditions:

- Undifferentiated fever
- DF
- DHF
- Expanded dengue syndrome (rare)

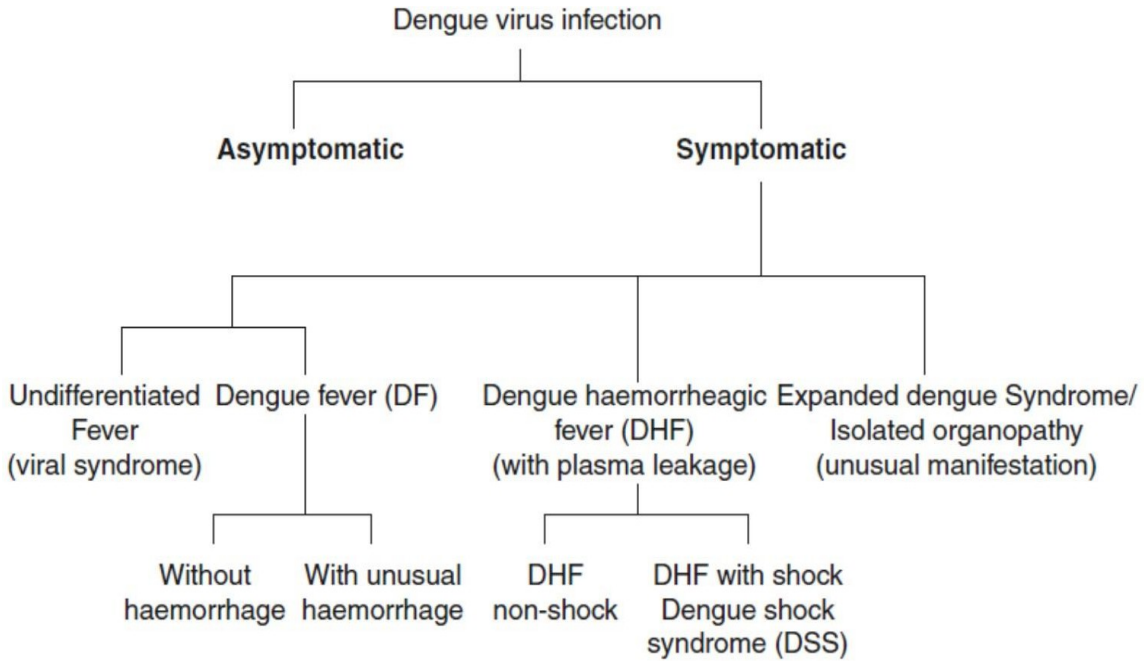


Figure 12: WHO and SEARO 2001 or WHO 1999 criteria for dengue classification. (Source: adopted from WHO criteria for dengue classification)

3.1.1 Asymptomatic Infection:

Majority of dengue virus infections are asymptomatic. However, age appears to influence the prevalence of symptomatic disease. The majority of infections in children under age 15 years are asymptomatic or minimally symptomatic.

3.1.2 Symptomatic Infection

3.1.2.1 Undifferentiated fever

Some of the patients infected with dengue virus, especially for the first time (i.e. primary dengue infection), may develop a nonspecific febrile illness with mild symptoms which are indistinguishable from other viral infections.

3.1.2.2 Classical Dengue fever (DF)

A proportion of patients infected with dengue virus develop classical dengue fever characterized by high fever, severe headache, retro-orbital pain, myalgia, arthralgia and rashes. Leucopenia and thrombocytopenia are usually observed. Although DF is usually benign, it could be an incapacitating disease due to severe headache and musculo-skeletal pains (break-bone fever). Occasionally, unusual haemorrhage such as gastrointestinal bleeding, hypermenorrhea and massive epistaxis may occur.

Fever

- Sudden onset, high grade, continued.
- The body temperature is usually between 39 °C and 40 °C (102° F to 104° F).
- The fever may be biphasic, lasting 2–7 days in the majority of cases.

Rash

first 2 to 3 days - Diffuse flushing or blanching erythema may be seen on the face, neck and chest

Third and fourth day - a conspicuous rash that may be maculo-papular or rubelliform.

Afebrile period or defervescence - Some patients have a confluent erythematous or petechial rash with small areas of normal skin, described as “isles of white in the sea of red” may appear over the dorsum of the feet, on the legs and on the hands and arms. Skin itching may be observed.

Rash in dengue fever:

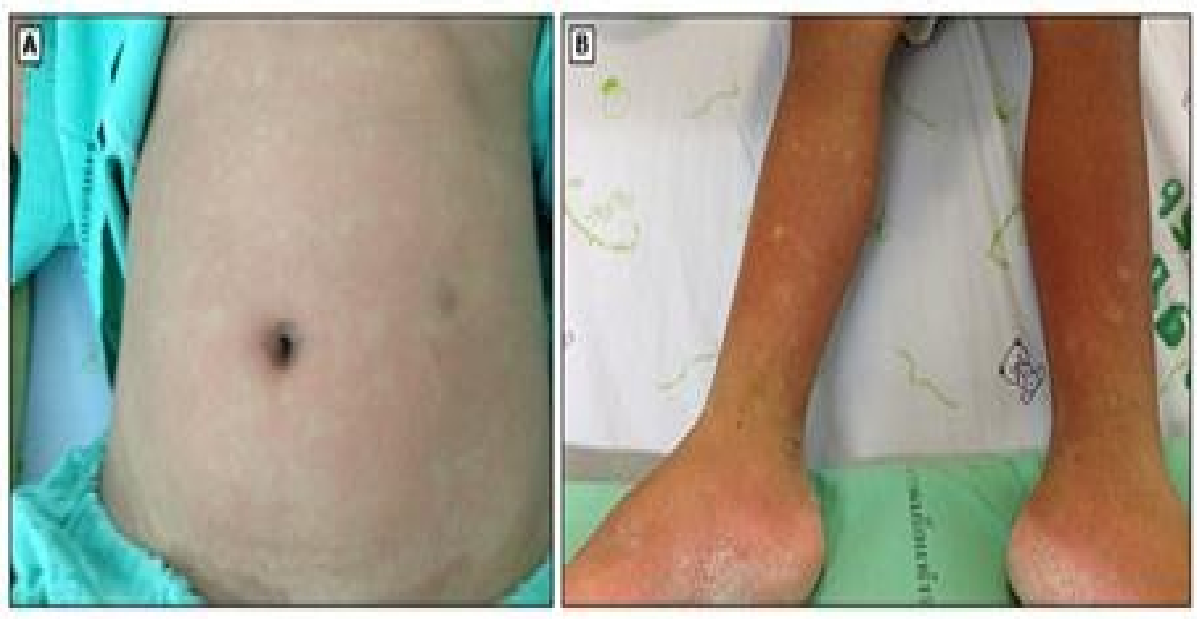


Figure 12: Dengue rash

(A) Undifferentiated macular or maculopapular rash may occur over the face, thorax, abdomen, and extremities during the acute phase of dengue. The rash is typically macular or maculopapular and may be associated with pruritus.

(B) Convalescent rash is characterized by confluent erythematous eruption with sparing areas of normal skin. It is often pruritic. The rash typically occurs within one to two days of defervescence and lasts one to five days.

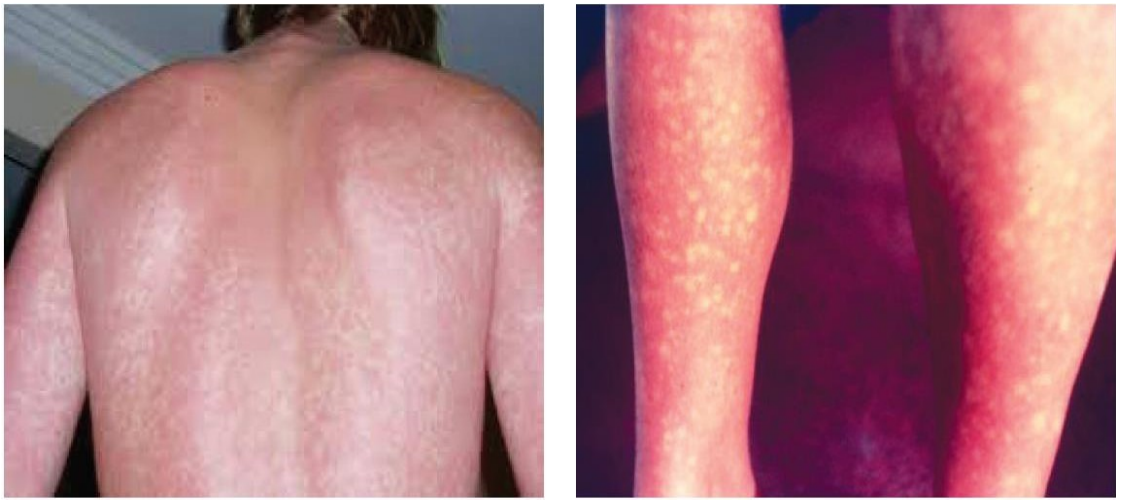


Figure13: Isles of White in the Sea of Red.

Warning signs of dengue fever: (CDC 2024)

- Intense continuous abdominal pain or pain when palpating abdomen
- Persistent vomiting (≥3 episodes in 1 hr or ≥4 in 6 hrs)
- Fluid accumulation (pleural effusion, ascites, or pericardial effusion)
- Mucosal bleeding (gums, nose, vagina [metrorrhagia or hypermenorrhea], kidney [macroscopic hematuria])
- Altered mental status (irritability, drowsiness, Glasgow Coma Scale score <15)
- Hepatomegaly (≥2cm below costal margin)
- Progressive increase of the haematocrit (in at least 2 consecutive measurements taken 6 hours apart

3.1.2.3 Dengue Haemorrhage Fever (DHF)

DHF occurs in a small proportion of patients with dengue infection. Most DHF patients present with acute onset of high fever and associated symptoms similar to DF in the early febrile phase. **Plasma leakage and abnormal hemostasis** are the hallmarks of DHF which usually occurs around the defervescence (settling of fever). There is a possibility of developing shock (dengue shock syndrome) if the leakage is severe or due to significant bleeding in addition to leakage. Therefore, patients with probable dengue illness should be closely monitored as it can develop DHF with time. For efficient management of DHF it is important to understand its natural history and its dynamic nature. Clinical course of DHF is stereotypic and consists of three phases:

- Febrile phase
- Critical phase (leakage phase)
- Convalescent phase

Note: Equilibrium phase is seen in some cases after critical phase

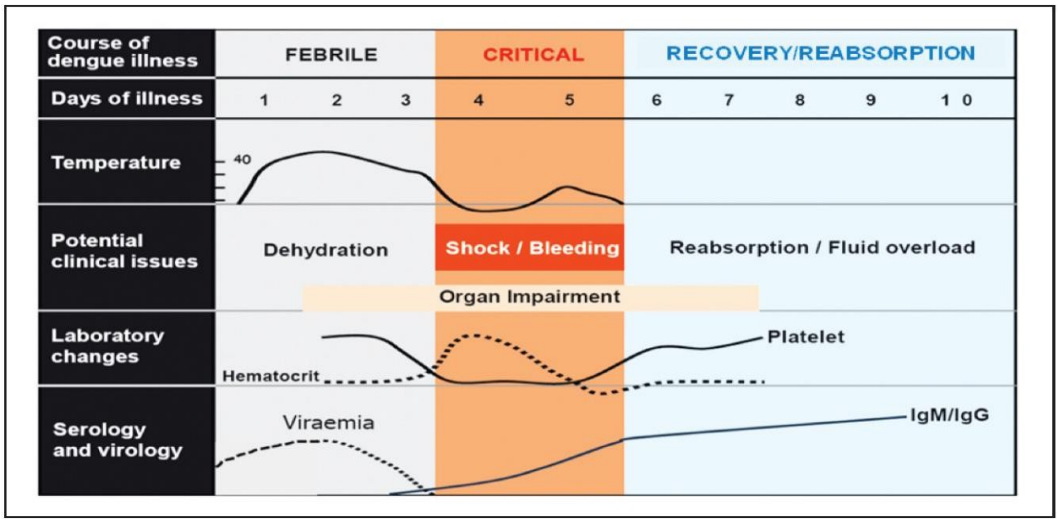


Figure 14: Three phases during course of DHF. Source: CPG Management of Dengue Infection in Adults (Third Edition) 2015.

The figure depicts the course of dengue illness over 10 days, divided into three phases: febrile, critical, and recovery/reabsorption. It illustrates changes in temperature, potential clinical issues, laboratory changes, and serology/virology markers during each phase.

Febrile phase:

Febrile phase is characterized by continuing high fever lasting for 3-5 days. Other features seen in the febrile phase include facial flushing/diffuse blanching erythema of the skin, myalgia, arthralgia, headache, nausea and vomiting. Some patients may have sore throat, diarrhoea, injected pharynx, conjunctival injection and tender posterior cervical lymphadenopathy. Mild haemorrhagic manifestations can occur. Leucopenia (WBC<5000 mm^3) and mild thrombocytopenia(<150,000/mm^3) are common in the late febrile phase. Tender hepatomegaly and significant (moderate to severe) elevated transaminases (ALT, AST) in febrile phase favours the possibility of developing DHF. A smaller rise in Hct/PCV which may be seen in the febrile phase of the disease is due to dehydration

Critical phase (leakage phase):

The critical phase is heralded by the onset of plasma leakage. Plasma leakage occurs due to capillary permeability. This usually starts after the 3rd day of fever (usually around the 4th or 5th day of illness) with defervescence (settling of fever). However, some patients may enter the critical phase while having high fever.

Evidence of Plasma Leakage:

- A gradual rise of Hct from the baseline (>10%) is suggestive of plasma leakage while a 20% rise of Hct from the baseline is indicative of significant plasma leakage.
- Plasma leakage in DHF is due to increased capillary permeability and it is transient and usually lasts for 24-48 hours.
- Evidence of ascites or pleural effusion.

Fluid in pericardial space is rare. The reason for selective plasma leakage to pleural and peritoneal spaces is unexplained but liver involvement in dengue infection may have a role. With the leakage of plasma there will be haemoconcentration which will manifest as an increase in Hct/PCV.

However, coexisting bleeding in addition to plasma leakage will obscure the expected rise in Hct/PCV. The point of care ultra sonography of the abdomen and the chest is a useful method for detecting plasma leakage.

Other evidence which may be suggestive of plasma leakage are a decrease in serum albumin (<3.5g/dl) and non-fasting serum cholesterol (<100mg/dl). But these may vary depending on the baseline of individual.

The degree and the rate of plasma leakage in DHF can vary. It can be minimal in some patients while in others it can be very significant. Plasma leakage usually starts slowly, increases gradually, slows down and then ceases altogether at the end of critical phase (usually within 48 hours from the onset). Plasma leakage is variable in patient to patient. In patients who have gone into shock status, the leakage may continue for a longer period than 48 hours.

Those who have severe leakage can develop shock when a critical volume of plasma is lost. If the shock is prolonged consequent organ hypo-perfusion will result in progressive organ impairment, especially liver impairment, metabolic acidosis and disseminated intravascular coagulation (DIC) which often lead to massive bleeding.
Incidence of acute liver failure in people with dengue infection is about 2 % but the mortality rate of dengue-associated acute liver failure is almost 50 %. (Level 5)

Haemorrhagic manifestations are not essential for the diagnosis of DHF in the presence of objective evidence of plasma leakage. However, the term “DHF” is retained because these patients have abnormal haemsotasis and the possibility of developing overt or concealed bleeding during the course of illness

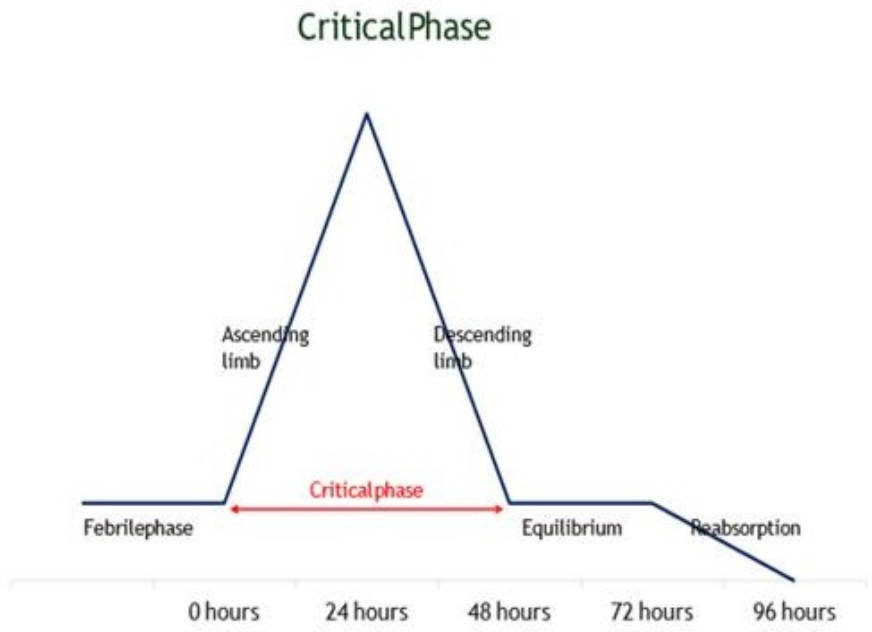


Figure 15: Critical phase (Source: National Institute of Infectious disease – IDH/Sri Lanka)

The diagram outlines the progression of events over time, marked in hours, and includes key stages such as the febrile phase, the ascending limb leading to the critical phase, the descending limb, equilibrium, and reabsorption

Skill Test: Tourniquet Test and Capillary Refill Time to identify critical phase.

Tourniquet Test:

The tourniquet test is part of the new WHO case definition for dengue. The test is a marker of capillary fragility and it can be used as a triage tool to differentiate patients with dengue fever from other febrile illness. Systematic reviews and meta-analyses show the tourniquet test has a marginal benefit for diagnosing dengue infection alone. (Level1)

How to do a Tourniquet Test?

1. Measure the blood pressure and record it, for example, blood pressure is 100/70 mmHg
2. Inflate the cuff to a point midway between SBP and DBP and maintain for 5 minutes. (100+70)/2= 85 mm Hg
3. The pressure is released for at least one minute and the skin below the cuff is examine for petechiae. See image at right
4. A finding of 10 or more petechiae in one square inch area considered positive. In DHF, the test usually gives a definite positive result when there is 20 petechiae per 1 inch with a sensitivity of more than 90%

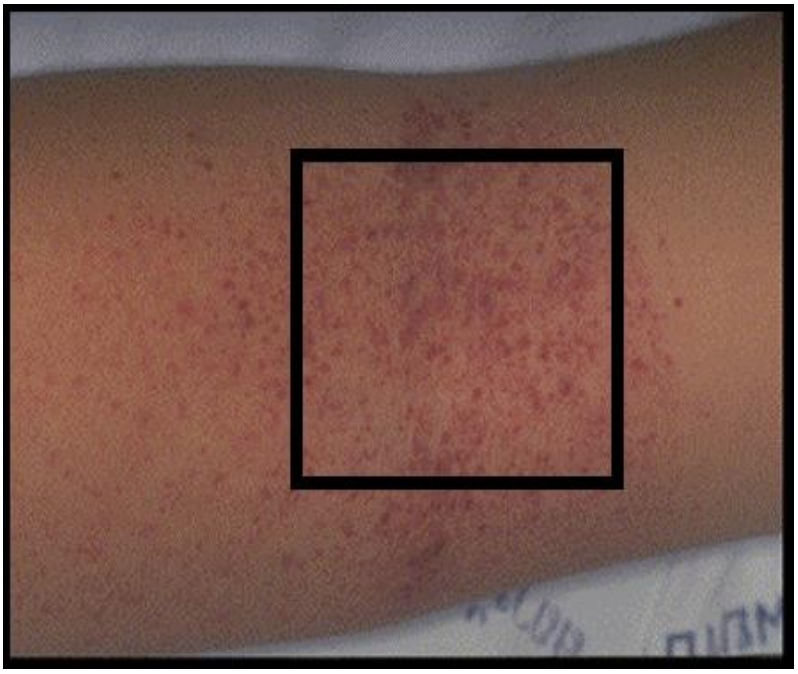
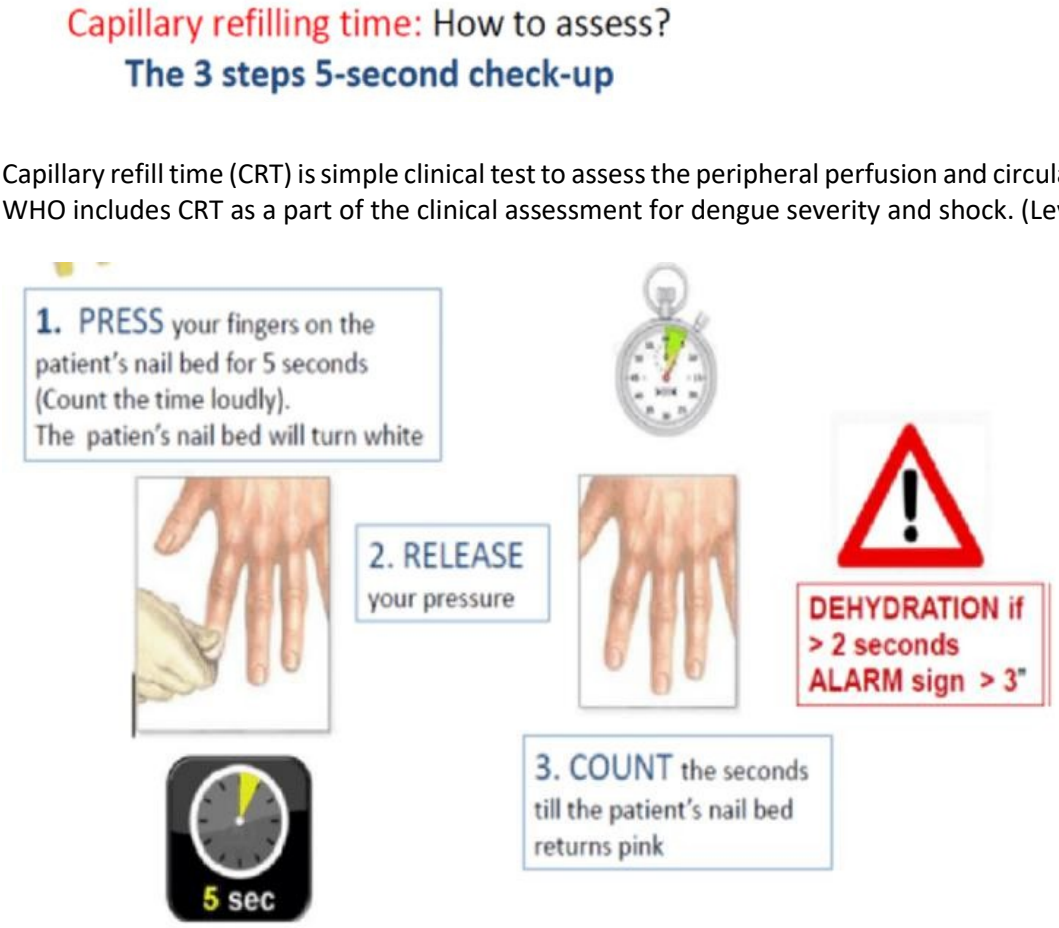


Figure 16: Presence of petechiae in tourniquet test.

Positive tourniquet test with greater than 10 petechiae per one square inch

Capillary Refill Time



Capillary refill time (CRT) is simple clinical test to assess the peripheral perfusion and circulation status. WHO includes CRT as a part of the clinical assessment for dengue severity and shock. (Level 6)

Figure 17: How to assess capillary refilling time at the triage (Note: Finger should be held at heart level) (Source: Samuele Caruggi, et al : Pediatric Dehydration Assessment at Triage)

Identifying the onset and end of the critical phase is important for fluid management.

- Early detection of the critical phase
- Dropping of platelet count below 100,000 is an early indicator of leaking
- Rapid drop of platelet count can occur
- Progressive rising of PCV towards10- 20% above baseline
- Gradual reduction of UOP
- Ultrasound evidence of leaking

Medical complications during the critical phase include the following:

- Hypovolemic shock from plasma leakage
- End organ impairment due to prolonged shock
- Severe haemorrhage
- Encephalopathy

	D3 M	D4 M	D4 E	D5 M	D5 E	D6 M	D6 E	D7 M	D7 E
WBC	3.2	2.7	1.7	2.9	3.7	4.5	6.1	7.0	8.3
N	60%	54%	51%	41%	31%	26%	33%	36%	43%
L	40%	45%	48%	56%	68%	71%	66%	64%	55%
HCT	36	36	36	43	49	47	40	36	36
Platelets	154	122	108	56	22	18	12	08	21
	Febrile phase			Critical phase				Convalescence phase	

Figure 18: Monitoring chart of a dengue patient where sequential changes in different parameter of CBC has been shown.

3.1.2.4 Dengue shock syndrome (DSS)

Circulatory shock is a life-threatening condition of circulatory failure, causing inadequate oxygen delivery to meet cellular metabolic needs and oxygen consumption requirements, producing cellular and tissue hypoxia. In DSS inadequate tissue perfusion is mainly due to reduction in the intravascular volume due to plasma leak or haemorrhage.

- Massive leakage ⟶ Hypovolaemia ⟶ Shock
- Patients might develop shock around the peak of the critical phase (18 – 24 hours)
- Can occur early due to dehydration and bleeding
- If the diagnosis is delayed can lead to prolong shock
- If shock lasts for > 4 hours it can lead to liver failure
- Prolonged shock can lead to multi organ failure, bleeding and death.

Clinical signs of dengue shock syndrome (features of circulatory failure)

- Cool extremities, cyanosis, capillary refill time delayed.
- Tachypnoea or Kussmaul's breathing (rapid, deep breathing)
- Tachycardia, weak pulse,
- Narrow pulse pressure: pulse pressure ≤20 mmHg with increased diastolic pressure, e.g. 100/80 mmHg.
- Hypotension by age, defined as systolic pressure <80 mmHg for those aged <5 years or 80 to 90 mmHg for older children and adults.
- Reduced urinary output.
- Lethargy or restlessness (which may be a sign of reduced brain perfusion)

Classification of DSS:

- Compensated Shock or Normotensive Shock (circulatory failure manifested by narrow pulse pressure is defined as pulse pressure equal or <20 mm Hg)
- Decompensated shock or hypotensive shock (SBP<90mmHg or reduction of SBP>20% or mean BP<60)
- Profound shock (BP and pulse unrecordable)

Clinical symptoms and signs in compensated and decompensated shock

Normal Circulation	Compensated shock	Decompensated /Hypotensive shock
Clear conscious	Clear conscious. Shock can be missed if you don't touch the patient	may be restless, aggressive, or lethargic
Capillary refill time (<2 sec)	Prolonged capillary refill time (>2 sec)	Prolonged capillary refill time
Extremities: warm & pink	Cold extremities	Cold, clammy extremities (skin may be mottled)
Peripheral pulses: good volume	Peripheral pulses: weak & thready (difficult to feel)	Feeble or absent peripheral pulses
Heart rate: normal for age	Tachycardia	Tachycardia
Blood pressure: normal for age	Normal systolic pressure with raised diastolic pressure.	Profound shock /unrecordable BP.
Pulse pressure: normal	Narrowing Pulse pressure (<20 mmHg)	Pulse pressure variable
Respiratory rate: normal for age	Tachypnoea	hyperpnoea/ Kussmaul's breathing
Urine output: adequate	Urine output -reduced	Oliguria or anuria

Table 1: Difference between compensated and decompensated shock.

Source: Clinical practice guidelines MOH/P/PAK/309.15 (GU) management of dengue infection in adults (Revised 3rd edition). 2015

Note: Profound shock: altered mental status, very prolonged capillary refilling time, absent peripheral pulse, unrecordable BP, Kussmaul's breathing, anuria.

Equilibrium phase:

In some patients, after the 48 hours of critical phase before they go into convalescent phase, a period of equilibrium may be seen where plasma leakage and reabsorption both occur in equal state. In this stage symptoms and signs of recovery may not be seen for several hours. Their urinary output (UOP) may be marginal (0.5-1 ml/kg/hr) and Hct/PCV may fluctuate. In such patients' critical phase monitoring should be continued unless they show features of convalescence. However, patients will remain stable and will not need any intervention.

Convalescent phase (recovery phase):

convalescent phase begins at the end of critical phase and usually lasts for 2-5 days. There will be reabsorption of extravasated fluid, during this period.

Features of convalescent phase:

- Improved general wellbeing and improved appetite.
- Appearance of convalescent rash ('White islands in red sea' appearance)
- Generalized itching (more intense in palms and soles)
- Haemodynamic stability
- Bradycardia (seen in some patients)
- Rash
- Diuresis
- Stabilization of Hct (may be lower than baseline due to reabsorption of extravasated fluid)
- Rise in the platelet count

However, if excessive amounts of intravenous (IV) fluids have been used in the critical phase there could be signs of fluid overload, such as respiratory distress due to pulmonary oedema or large pleural effusions.

3.1.2.5 Expanded dengue syndrome (EDS)/ Isolated organopathy:

EDS is a term announced by the WHO in 2011 to cover the uncommon expressions of dengue involving severe damage to the liver, kidneys, bone marrow, heart, or brain. Certain high-risk groups such as pegnant women, infants, elderly groups, and patients with coronary artery disease, hemoglobinopathies, and immunocompromised individuals are particularly susceptible to developing EDS. Organ impairment develops without evidence of fluid leakage and therefore do not necessarily fall into the category of DHF. These conditions are very uncommon and need to be managed according to the involved organ. However, these manifestations, if seen in DHF patients are mostly a result of prolonged shock leading to organ failure and therefore such patients should not be categories as patients with expanded dengue syndrome.

Early identification of bleeding (DF/DHF):

Bleeding is a common complication in dengue illness and is multifactorial. It can occur in both DF and DHF patients. In pediatric age groups, bleeding usually occurs after prolonged shock. However, in adults, bleeding can occur without shock. In some patients bleeding can be overt in the form of haematemasis, melaena, and menorrhagia. However, in most of the patients bleeding is occult.

Suspect bleeding in Dengue patients having following features:

- Unexplained tachycardia
- Normal or low PCV/Hct with unstable vital signs and/or reduction of urine output.
- Normal Hct in the background of thrombocytopenia.

Key features of dengue:

Dengue fever

- High, continued fever for 2- 7 days
- Headache
- Myalgia
- Arthralgia/ bone pain (break-bone fever)
- Rash
- GIT manifestation: Nausea, vomiting, diarrhea
- Hemorrhagic manifestations
- (mild, unusual haemorrhage)
- Leukopenia (WBC <5,000
- cells/mm3)
- Platelet count ≤150,000 cells/mm3
- Rising Hct 5-10%

Diagnosis:
Tourniquet test positive + WBC ≤ 5.000 cells/cu.mm (positive predictive value = 83%)

Dengue Hemorrhagic Fever (DHF)

- High, continuous fever 2-7 days.
- Hemorrhagic manifestations: tourniquet test positive, petechiae, ecchymosis, purpura, epistaxis, hematemesis etc.
- Liver enlargement ±
- Shock±
- Platelet counts ≤100,000 cells/mm3.

Evidence of plasma leakage:

- Pleural effusion,
- Ascites,
- Rising Hct ≥ 20% (Hct may remain normal when overt or covert bleeding present in leakage phase)
- hypoalbuminemia (serum
  - albumin < 3.5 gm % or <4gm% in obese patients)
- Peri-cholecystic fluid collection
  - evidenced by USG

Dengue shock syndrome (DSS)

- Evidence of plasma leakage+ evidence of circulatory failure
- Platelet counts ≤100,000 cells/mm3.

Evidence of plasma leakage (Please see the previous box)

Evidence of circulatory failure:

- Cold/cold clammy skin,
- CRFT>2 Sec,
- tachycardia,
- weak pulse,
- narrow pulse pressure <20, hypotension

3.2 Differential Diagnosis of Dengue Fever

Fever that has similar clinical feature of dengue like fever, rash, body ache, headache are its differential diagnosis. Clinical presentation of following infections has similarity with dengue fever: Infection by

Arboviruses: Chikungunya virus, Zika virus

Other Viral Infection: Measles, rubella and other viral exanthems, Epstein-Barr virus (EBV), Enteroviruses, Influenza, Hepatitis A, Hanta virus.

Bacterial diseases: Meningococcemia, Leptospira, Enteric fever, Melioidosis, Rickettsial disease, Scarlet fever, Sepsis.

Parasitic Disease: Malaria.

Dengue, Chikungunya and Zika

Dengue, chikungunya, and Zika are all mosquito-borne viral diseases that can cause similar symptoms, such as fever, headaches, muscle and joint pain.

Clinical signs and symptoms and laboatory findings to differentiate dengue, zika and chikungunya.

Certainty of the evidence	Signs and Symptoms		
	Dengue	Chikungunya	Zika
HIGH (findings that differentiate them)	- Thrombocytopenia - Progressive increase in hematocrit - Leukopenia	Arthralgias	Pruritus
MODERATE (findings that probably differentiate them)	- Anorexia or hyporexia - Vomiting - Abdominal pain - Chills - Hemorrhages (includes bleeding on the skin, mucous membranes, or both)	Rash Conjunctivitis Arthritis Myalgias or bone pain	Rash Conjunctivitis
LOW (findings that may differentiate them)	- Retro-ocular pain - Hepatomegaly - Headache - Diarrhea - Dysgeusia - Cough - Elevated transaminases - Positive tourniquet test	Hemorrhages (includes bleeding on the skin, mucous membranes, or both)	Adenopathies Pharyngitis or odynophagia

Guidelines for the Clinical Diagnosis and Treatment of Dengue, Chikungunya, and Zika. Washington, D.C.: Pan American Health Organization; 2022
License: CC BY-NC-SA 3.0 IGO. https://doi.org/10.37774/9789275124871

Table 2: Table showing clinical differentiation among dengue, chikungunya and zika.

Chapter-4

4.1 Laboratory Investigations for Dengue:

Dengue (DEN) virus, which has 4 distinct serotypes, i.e. DEN -1, DEN-2, DEN-3 & DEN-4. Early laboratory confirmation of clinical diagnosis may be important because some patients progress within a short period from mild to severe disease and sometimes to death.

4.1.1 Laboratory Tests for Diagnosis and Monitoring

The management of dengue cases is based on both clinical features and laboratory evaluations. Suggestive laboratory test of dengue cases management is following:
CBC and NS-1 Ag/ Anti-Dengue Ab should be done in all suspected dengue patients at their first visit depending on the day of presentation.

4.1.1.1 Complete Blood Count (CBC):

WBC counts: **Leucopenia** is common in both adults and children with DF (Level 1) and has an important diagnostic implication in early period. The change in total white cell count (≤5000 cells/mm^3) and ratio of neutrophils to lymphocyte (neutrophils <lymphocytes) is useful to predict the critical period of plasma leakage (Level 6). NLR (Neutrophil Lymphocyte ratio) <2 strongly correlates with low platelets indicating severity of disease and reversal of NLR >2 correlates with improvement of disease (Level 6). This finding precedes thrombocytopenia or rising haematocrit. These changes seen in DF and DHF.

Total Platelet count (PC): **Thrombocytopenia** is observed in patients with DF & DHF. The level of platelet count is correlated with severity of DHF (level 1). Thrombocytopenia (<100,000/mm^3) usually precedes/accompanies plasma leakage.

Haematocrit (Hct): Haemotacrit is most important tool in diagnosing and guiding effective treatment of dengue patient(Level 5). Approximately 5-10% increase in Hct may occur due to high fever, anorexia and vomiting. A sudden rise in haematocrit is observed simultaneously or shortly after the drop in platelet count. Rising haematocrit more than 10 % indicates starting plasma lekage and rising haematocrit by 20% from the baseline indicates established plasma leakage. For example, rising haematocrit from 35 to 42 indicates 20% rise. In critical phase / leaking phase haematocrit may not rise due to concomitant concealed or overt bleeding. During plasma leakage period Hct should be monitored at least twice daily and more frequently considering the clinical scenario, If facilities available. Bedside haematocrit is suggested in admitted patients. There is no data but it assumes that base line Hct in child, adult female and adult male are 35%, 38% and 40% respectively.

4.1.1.2 Dengue antigen and antibody tests:

Detection of antigen: dengue NS1 antigen (non-structural protein 1):

- The Dengue NS1 antigen usually positive on first day of illness.
- This antigen test may become negative from 4-5 days of illness.

Note: The sensitivity, specificity, positive, and negative predictive value of rapid dengue NS1 antigen test were 81.5%, 66.7%, 78.2%, and 71.1%, respectively whereas that of NS1 ELISA were 89.9%, 100%, 100%, and 94%, respectively. Concordance of Rapid NS1 and NS1 ELISA with PCR was 75.5% and 94%.

Dengue IgM /IgG antibody test (MAC ELISA or enzyme-linked immuno-sorbent assay or Rapid Immnuno Chromatomatic Test):

- Anti-dengue IgM can be detected after 5 days of the onset of fever and reaches highest level after 7 days of fever.
- It can be detected up to 1-3 months after dengue fever.
- In primary dengue infection- anti-dengue IgM will be detected earlier than IgG which (IgG) will appear on the 9th or 10th day of illness. Level of this IgG may persist at low levels for life long, indicating past dengue infection.
- In secondary dengue infection- higher levels of anti-dengue IgGand lower levels of anti-dengue IgM are detected at 2nd week. The anti-dengue IgG levels detected lifelong.

4.1.1.3 Nucleic Acid Detection:

- Dengue diagnosis is confirmed by detecting DEN viral RNA using reverse transcriptase polymerase chain reaction (RT-PCR; This test is usually positive within 5 days of onset of symptoms. It can also be detected by traditional PCR.)

4.1.1.4 Dengue Virus Isolation:

- This test is usually done for research purpose and are not readily used for routine diagnostic test.
- Dengue virus isolation in cell culture (Vero, C6/36 cell lines) done from serum, plasma and leucocytes is the most definitive test for dengue infection, which can be usually accomplished in majority of cases if the sample is taken in the first five days of onset of symptoms.
- Isolation of dengue virus also from CSF or autopsy samples.
- Detection of dengue virus or antigen in tissue, serum or cerebrospinal fluid by immunohistochemistry, immunofluorescence
- Detection of dengue virus genomic sequences by reverse transcription- polymerase chain reaction.

4.1.2 Biochemical Tests:

Serum AST (SGOT) and ALT (SGPT): Transaminases are commonly abnormal in dengue fever where classically AST is more than ALT. Elevated aspartate aminotransferase levels were strongly associated with severe dengue. (Level 1)
In Classical Dengue fever AST/ ALT may be slightly raised (2-5 times of upper limit of normal) but in dengue haemorrhagic fever ALT and AST may be 5 to 15 times the upper limit of normal. Serum Albumin <3.5 gm/dl indicates plasma leakage.

Additional following test might be needed depending on the severity of clinical scenario:

- Serum Creatinine/Blood urea nitrogen (BUN) may be elevated in prolonged shock.
- Serum Electrolyte: Hyponatremia is frequently observed in DHF/DSS
- VBG (venous blood gas analysis): Metabolic acidosis is frequently found in cases with prolonged shock
- RBS may be low in DSS
- Serum calcium: Hypocalcaemia (corrected for hypoalbuminemia) has been observed in DHF.

4.1.3 Coagulation Profile:

Assays of coagulation and fibrinolytic factors show reduction in DSS cases. Activated Partial thromboplastin time (aPPT) and prothrombin time (PT) are prolonged in about half and one third of DHF cases respectively. Thrombin time (TT) is also prolonged in severe cases.

4.1.4 Other tests:

- Chest X-Ray: Pleural effusion on X-ray in dengue indicates fluid accumulation.
- Ultrasonography: To detect pleural effusions or ascites, it is essential to obtain objective evidence of selective capillary plasma leaking into the chest and abdominal cavities.
- Urine R/M/E: Albuminuria/Hematuria may be present
- Other tests might be done to exclude other diagnosis such as ICT for malaria, microscopy for malaria, Blood culture to exclude enteric fever.
- ECG, Echocardiography, Troponin I, CK-MB if myocarditis is suspected.
- CSF: In dengue encephalitis.

N.B: It should be noted that the use of medications such as analgesics, antipyretics, anti- emetics and antibiotics can interfere with liver function and blood clotting.

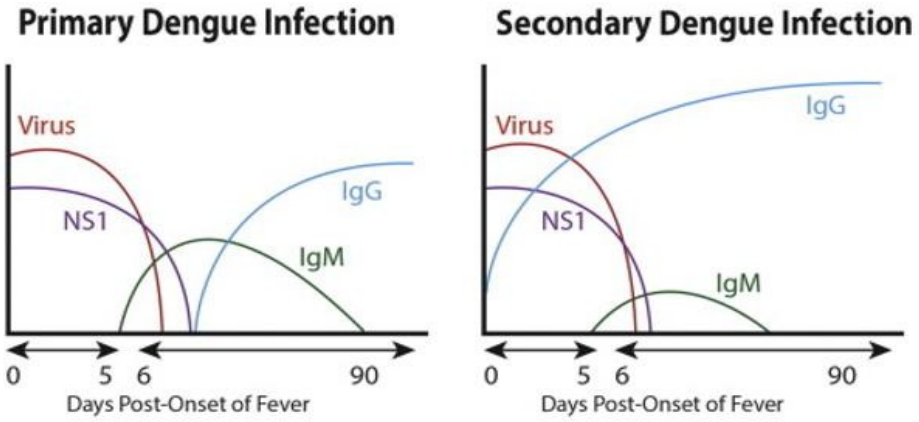


Figure 19: Changes in serological markers used in dengue diagnosis during primary and secondary dengue infections

4.1.5 Time and frequency of investigation:

Within 5 days: CBC, Haematocrit, Dengue NS1 antigen, SGOT, SGPT

- These tests should be done during first consultation to get the baseline characteristics like Haematocrit and complete blood count if the patient presented within 5 days of fever.
- Follow up testing may be done on 1st afebrile day, but should be done daily once DHF is suspected.
- A regular haematocrit is more important for management than the platelet count
- Even in severe dengue especially with shock haematocrit to be monitored 3 hourly or more frequently is crucial for management. (According to monitoring chart; Annexure)
- Once the platelet count begins to rise and reaches ≥ 50,000/mm^3,daily lab evaluations may be discontinued.

4.1.6 Role of point of care (POC) ultrasound in dengue:

Point of care ultrasonography is not essential to manage dengue patient but it has now evolved into an important and reliable method of diagnosing plasma leakage objectively in clinically suspected DHF patients. (Level 4)

There are many advantages of POC ultrasound. It can be done at the bedside on unprepared patients and can be repeated frequently if needed. POC ultrasound can also be used to predict the probable duration of the critical phase.

Areas of interest of POCS in dengue

Main areas:

- Gallbladder - gallbladder wall thickening and appearance of para cholecystic fluid
- Fluid in the hepato-renal pouch
- Fluid in right pleural cavity
- Fluid in the pelvis (recto vesical pouch)

Additional areas:

- Fluid in left pleural cavity
- Fluid in pericardial space
- Fluid in spleeno-renal angle.

When should you perform POC ultrasound in dengue:

- When there is a suspicion of DHF (based on clinical, hematological or rarely biochemical findings)
- Despite the negative initial scan, if there is a clinical suspicion the POC ultrasound scan
- should be repeated at frequent intervals.
- Once the fluid leakage is detected and the onset time is defined, there is no need to repeat the scan unless there is a clinical deterioration.

Findings on point of care ultrasound in DHF:

- The presence of gall bladder wall oedema with no fluid around it, is not a feature of plasma leakage. However, this generally precedes plasma leakage. Therefore, if gall bladder wall is detected, repeat scan is warranted in 3-6 hours to identify possible plasma leakage.
- Gall bladder wall oedema with a thin rim of fluid around it (PCF- peri cholecystic fluid) could be the earliest sonographic finding of plasma leakage. To see the progress of leaking, repeat scan in 3-6 hours.
- A thin rim of fluid in hepato-renal recess indicates a minimum of **six hours** has elapsed since the beginning of plasma leakage.
- Fluid in the peritoneal cavity, among bowel loops and in the pelvis, indicates a minimum of twelve hours have elapsed since the beginning of plasma leakage
- Fluid in the pleural space, is commonly seen on the right side and indicates minimum of twelve hours have elapsed since the beginning of plasma leakage.
- In a patient where bilateral pleural effusions and ascites are seen; implies that the patient is in the latter part of the critical phase and more than 24 hours have lapsed from the onset. You may measure the thickness of fluid in each area for subsequent comparison, especially if there is a clinical deterioration.

Note: When taken together with the duration of illness, drop of platelet count and changes in haemodynamic parameters and urine output, the ultrasound findings enable the clinicians to estimate the duration of the critical phase

POINT OF SONOGRAPHIC INTEREST	EXPECTED FINDING	PRESUMED TIME OF ONSET OF LEAKING	SPECIAL NOTES
Gallbladder	Wall thickening (normal 3mm)	Not started	May be seen in DF (without DHF), hepatitis, gall bladder or colonic infections
Gallbladder	Para cholecystic fluid	May herald leaking, Repeat in 3 hours	May be seen in acute cholecystitis
Morrison's pouch (MP)	Fluid	More than 6 hours	
Morrison's pouch +right pleural cavity	Fluid	More than 12 hours	
Morrison's pouch + right pleural cavity + left pleural cavity	Fluid	More than 24 hours	

Table 3: POCUS findings on different time of critical phase.

Available Dengue Diagnostic Tests at Different Level of Health Care Centers:

Primary Health Center: For diagnosis and surveillance, rapid tests for dengue-specific IgM/IgG and NS1 antigen should be utilized at the primary health care level.

Secondary Health Center: At district health centers, both ELISA and rapid tests for detecting antigens and antibodies can be conducted.

Tertiary Health Center: All diagnostic methods, including virus isolation, nucleic acid detection, and all serological techniques, should be accessible at referral centers.

	Clinical Sample	*Diagnostic Method*	*Methodology*	*Time of Result*
Virus Detection and its component	Acute Serum (1-5 days of fever) and necropsy tissue	Viral Isolation	Mosquito or mosquito cell culture inoculation	One Week or more
			RT-PCR & Real Time RT PCR	1 to 2 days
		Nucleic Acid Detection	NS1 Antigen Rapid Test	Minutes
			NS1Ag ELISA	1day
		Antigen Detection	Immunohistochemistry	2-5 days
Serological response	Paired Sera (Acute Serum from 1-5 days and second serum from 15-21 days after)	IgM or IgG Sero -conversion	ELISA HA	1-2 days
			Neutralization Test	Minimum 7days
	Serum after 5 days of fever	IgM Detection (Recent Infection)	ELISA	1 or 2 days
			Rapid Test	Minute
		IgG detection	IgG, ELISA, HIA	1 or 2 days

Table 4 - Time & Frequency of Investigation

Method	Diagnostic Tools	Primary Health Care Center	District Health Center	Tertiary Level Health Center/ Reference Center
Virus isolation		-	-	Yes
Genome Detection		-	-	Yes
NS1 Antigen detection	Rapid Test	----	Yes	Yes
	ELISA	----	Yes	Yes
IgM Detection	Rapid Test	----	Yes	Yes
	ELISA	----	Yes	Yes
IgG Detection	ELISA	----		Yes
	IHA	----		Yes
	Neutralization assay	----		Yes

Table 5 - Dengue Diagnostic Service Delivery Level

ELISA=enzyme-linked immunosorbent assay; IgG=immunoglobulin G; IgM=immunoglobulin M; IHA = indirect haemagglutination; NS1 Ag = non-structural protein 1

	Method	Interpretation	Sample characteristics
Confirmed Dengue Infection	Viral isolation	Viral isolation	Serum (collected at1- 5 days of fever) Necropsy tissues
	Genome detection	Positive RT-PCR or positive real-time RT-PCR	
	Antigen Detection	**Positive NS-1 Ag**	
		Positive immunohistochemical	Necropsy tissues
	IgM sero -conversion	**From negative IgM to positive IgM in paired sera**	Acute serum (1–5 days) and convalescent serum (15–21 days) after first serum
	IgG sero -conversion	From negative IgG to positive IgG in paired sera or 4-fold increase IgG levels among paired sera	
Probable Dengue Infection	Positive IgM	**Positive IgM**	Single serum collected after day5
	High IgG levels	High IgG levels by ELISA or HI(≥ 1280) ELISA	

Table 6 - Confirmed and probable dengue diagnosis, interpretation of results and sample characteristics

Chapter-5

5.1 Dengue Case Definition

Suspected case: Acute febrile illness meeting clinical dengue criteria without confirmatory tests.

Probable Case: Acute febrile illness with serological diagnosis.

Confirmed Case: Laboratory confirmation through any one of the followings

- Positive RT-PCR or NS1 antigen test
- Positive immunohistochemistry from necropsy tissues
- Seroconversion (negative to positive IgM/IgG in paired sera)
- Fourfold rise in IgG in paired sera samples.

Severity Classification:

Dengue without warning signs: Fever (2-7 days) with two or more of the followings; nausea, vomiting, rash, aches and pains, positive tourniquet tests, or leucopenia (WBC <5000/mm^3)

Dengue with warning signs: Dengue fever with any one of the warning signs. **(page 28)**

Severe Dengue:

- Severe plasma leakage leading to shock (DSS) or fluid accumulation causing respiratory distress.
- Severe bleeding as per clinical evaluation
- Severe organ involvement (e.g. elevated AST/AST≥ 1000iu/L, impaired consciousness, or organ failure.

5.2 Outpatient Assessment and Management of a Patient with Dengue Fever.

Out-Patient Department:

Fever Corner - A triage center for febrile patients

Fever corner should consist of a **Triage Desk** where fever patients will be registered and assessed based on duration of fever.

- Then the patients can be seen by medical officers and managed accordingly.

In the present hyper-endemic setting in Bangladesh, dengue illness (DF and DHF) should be considered in any patient presenting with an acute febrile illness. Clinical evaluation of dengue is based on symptoms and signs. Basic investigations depend on day of illness. CBC and NS1 Ag up to day 5 and CBC and Dengue Antibody from day 6 onward will support the diagnosis.

Stepwise approach on outpatient management on dengue History:

- Date of onset of fever/ illness
- Date and time of last episode of fever
- Oral intake
- Warning signs
- Diarrhoea
- Bleeding including menstrual bleeding
- Change in mental status /seizure /dizziness
- Urine output (frequency, volume and time of last voiding)
- Other important relevant histories: drug history, comorbidities.

Physical examination:

- Mental status
- Hydration status
- Haemodynamic status
- Tachypnoea/ acidotic breathing/ pleural effusion
- Abdominal tenderness/ hepatomegaly/ ascites
- Bleeding manifestation

Investigation:

- CBC and Hct
- NS-1
- SGPT/SGOT
- CRP (level 4)

Besides checking clinical and lab parameter of dengue, proper history to be taken on comorbid condition, high risk for severe disease and adverse social condition of the patients.

Patients at high risk for more severe disease and its complications may need admission even without the above criteria.

- Pregnant women
- Elderly
- Obesity
- Patients on anticoagulants

Patients with comorbid conditions:

- Diabetes mellitus
- Hypertension
- Chronic renal failure
- Established liver disease
- Ischemic heart disease
- Solid organ/bone marrow transplant
- Active malignancies
- Hemolytic diseases and other haemoglobinopathies
- Peptic ulcer disease
- Patients on steroid or NSAID treatment
- Patients on anticoagulants

Patients with adverse social circumstances

- Age <1 year or >65 years
- Living alone or has poor access to healthcare facilities
- Lack of transportation
- Unstable housing
- Extreme poverty

All patients should be assessed in a stepwise manner to reach at the diagnosis, determine the severity and place of management.

At the end of evaluation, attending physician should be able to assess the patient on following points.

- Could this patient have dengue?
- Are there any warning sign?
- Is the patient having plasma leakage?
- Is the patient in shock?
- What is the haemodynamic and hydration status of the patient?
- Are there any co-morbidities or high-risk conditions or adverse social condition?
- Is hospitalization required immediately/early?

Fever	Warning Signs (WS)	Comorbid condition/High risk for severe disease/Adverse Social condition	Vital Signs (VS) & Urinary output (UOP)	Fresh CBC Finding	Patient Risk Status at the Time of Assessment	Hospitalization
Short duration of fever (or fever within last ≤48 hours)	Absent WS	Absent	Normal VS & Normal UOP	WBC low (Leucopenia) Platelet ≥100x10^9/L Hct: 35-40% or baseline	No immediate risk	Home management as well as followed up and assessed regularly.
	Present WS	Present	Derange VS Reduced UOP	WBC: decreasing Platelet ≤100x10^9/L Increasing Hct: Leaking Decreasing Hct: Bleeding	High risk.	Inpatient management

Table 7: Showing dengue patients who need inpatient/outpatient management.

Note:
➢ It is important to understand that vital signs and other parameters may be influenced by comorbidities and high-risk conditions (e.g., urine output in diabetes).
➢ Settling of fever is not a sign of recovery. Some patients will start plasma leakage around defervescence.

Home management of patients:

Patients without warning signs or coexisting conditions or social risk should get home based care through a register of dengue patient.

Recommended measures in home management:

- Adequate physical rest in comfortable clothing, and preferably under a mosquito net
- Control of temperature
  - ➢ Tepid sponging for fever
  - ➢ **Do not exceed 3 gm/day of paracetamol. (60mg/kg/24hrs in child)**
  - ➢ Warn the patient that the fever may not fully settle with paracetamol and advise not to take excess.
- Adequate Hydration
  - ➢ Ensure adequate oral fluid intake of around 2400 ml for 24 hours (if the body weight is less than 50kg, give fluids as 2ml/kg/hour for 24 hours) and it is better to spread this amount of fluid across the day.
  - ➢ This should consist of fluid such as ORS, green coconut water, other fruit juices or soup which has electrolytes rather than plain water
- Ensure adequate urine output. (Encourage to pass urine every 3-4 hours). It is useful to measure the urine output, if possible, and document with time, as any reduction in urine output can be easily identified.
- Patient should be informed about warning sign. **(page 28)**

- If the appetite is good, patients encouraged to take light and nutritious food.
- If the patient's appetite is poor, forced feeding should not be done, as taking adequate amounts of liquid is sufficient during illness.
- It is advisable to avoid red/ brown (i.e. dark) colored food (red dragon fruit, beet root)/ beverages to avoid confusion with blood-stained vomitus/ melaena)
- Anti-emetics and PPI/H2 receptor blockers if necessary.
- Avoid all NSAIDS (including COX-2 inhibitors) and steroids.
- Temporally withhold warfarin, aspirin, clopidogrel & dipyridamole, in patients who take these on long term basis. Take expert opinion where these drugs are necessary.

Follow up plan of home management

- Review daily with CBC. First CBC should be done at least at the beginning of the third day of fever/illness (preferably with SGOT and SGPT).
- These patients should be followed up until the patient become afebrile for 24-48 hours with stable clinical parameters. Usually, by seven days, most patients recover.
- If any indication for hospitalization appears within this follow up period, patient should get admitted to hospital.

Note: Written instruction to the patient/carer giver will be provided in Bengali regarding management of the patient. Instructions will be given in Bengali about investigations timing and how and when they can communicate with physician either physically or phone call/WhatsApp. (Instructions of patient/caregiver is in annexure).

Indications for immediate return for review / hospitalization

Advise patients to return to the hospital immediately, if they develop any of the following conditions:

- Clinical deterioration with settling of fever
- Inability to tolerate oral fluids
- Severe abdominal pain
- Lethargy or irritability / restlessness

Bleeding tendency like abnormal vaginal bleeding, blood vomiting, black tarry stool, bleeding from nose and gum.

Reduced urine output for the last 4-6 hours (<150-200 ml/ 4-6 hours if weight is 50kg or more)

- Cold and clammy extremities
- Difficulty in breathing.

Before transferring a patient from OPD to ward or another hospital after initial evaluation:

Following measures to be taken strictly

- Patient should be stabilized.
- All clinical findings, investigation results and treatment given should be clearly documented and sent with the patient.
- Reasons for transfer should be clearly documented in the transfer form
- Before transferring, the patient's condition should be briefed with the relevant management team of the hospital where the patient is being transferred.

Stabilization of a patient with DSS before admission/ transfer.

- Secure an IV line and administer a fluid bolus. Initiate IV fluids as per the clinical guidelines (See guidelines on fluid therapy in shock)
- If facilities available, take blood for CBC and PCV before starting the fluid bolus
- Check for hypoglycemia and correct if required
- Give oxygen to maintain a target saturation of >95%
- If the transfer is delayed, reassess and give another fluid bolus after discussing with the team at the transferring unit
- Consult with central Dengue team for any management support. Central dengue will be formed in every tire of health care facilities.

Counselling in outpatient department and record keeping by attending physician

- Discussion about the nature of the illness
- Information should be given regarding favorable outcomes of dengue,
- with appropriate management.

Develop an easy communication channel

- Maintain a patient record (with the doctor).
- Identify the patients' inherent fears

Leaflet of Dengue patient home management to be supplied to every patient: Annexure

5.3 Inpatient Management of Dengue Patient

Monitoring of dengue patients during hospital stay:

- Every inpatient should be assessed thoroughly, using the febrile/critical monitoring chart. (Annexure)
- If the patient is clinically stable on admission
- Measure body weight
- Assess vital signs
- Chart temperature 4 hourly
- Observe for evidence of bleeding, especially melaena or bleeding per vagina and quantify the amount of bleeding.
- Maintain an intake and output chart
- Measure the urine output (Normal: 0.5 -1 ml/kg/hr) (200-400 ml urine in 8 hours in a 50 kg person)
- Do an urgent CBC on admission and review the report early. Then repeat CBC daily or more frequently depending on different phase/situation of the patient.
- Inpatient PCV/Hct frequently as required.

Febrile phase monitoring:

- Ensure adequate fluid intake.
- Oral fluids are recommended if oral intake is good.
- If the patient is vomiting or dehydrated and not taking adequate oral
- fluid, consider intravenous (IV) fluids. Total fluid requirement (oral + IV) will depend on the degree of dehydration.
- The rate of infusion has to be reduced soon after the correction of dehydration.
- When IV fluids are needed during the febrile phase, use 0.9 % NaCl/ Hartman solution 5% dextrose in 0.9 % NaCl.
- Adequate physical rest.

Do not exceed 3 gm/day of paracetamol. (60mg/kg/24hrs in child) Avoid all NSAIDS and steroids.

- Temperature
- Vital parameters - pulse, blood pressure (both systolic and diastolic), respiratory rate, capillary refill time and urine output 4 hourly (may need more frequent monitoring depending on the clinical situation)
- Intake and output (maintain a urine output within 0.5 to 1 ml/kg/hr)
- CBC twice daily when platelet count is below 100000/mm^3
- Inpatient PCV or Hct twice daily or more frequently when patient is in shock

Annexure: Febrile monitoring chart

Identification and monitoring of critical phase by following points

- Clinical deterioration with defervescence of fever.
- Platelet count below 100×10^9/L
- A progressively rising Hct (>10-20%), may indicate that the patient is entering the critical period. A 20% rise indicates that there is a significant amount of plasma leakage.
- **A 30 % rise in the Hct is indicative of impending shock/ shock**
- Expected Hct rise will not be seen in a patient with plasma leakage if there is coexisting bleeding.
- Other features which may indicate that the patient is entering the critical phase are gradual reduction of urine output and new onset tender hepatomegaly.
- Rising pulse rate (>120/min with fever and >100/min without fever) disproportionate to the degree of fever and prolongation of capillary refill time may indicate that the patient is already in the critical phase.
- Normal or reduced Hct on the background of unstable vitals should always give suspicion of concealed bleeding.
- During the early phase of plasma leakage, many patients continue to have a fever with a lower intensity.
- The rate of leaking is highly variable from patient to patient. The leak usually starts slowly, increases gradually, reaching a peak usually around 24 hours then slows down and ceases altogether at the end the of leakage phase (usually within 48 hours from the onset).
- But sometimes it may last less than 48 hours or may extend even beyond 48 hours.
- Identifying the beginning and the end of the critical phase is a key factor in guiding

- fluid therapy in DHF. It is important to monitor patients hourly in leaking phase. Monitor patients every 15 minutes interval in case of shock.
- If the patient presents in shock, the patient may have been in critical phase for a significant period of time, probably up to 24 hrs. Therefore, there is a possibility that some patients will have approximately another 24 hours remaining in the critical phase.
- If a patient is already dehydrated during the latter part of the febrile phase (due to vomiting, diarrhea or lack of adequate fluid intake) and hydration is not corrected he or she might go into shock before 24 hours. In this instance the remaining duration of the critical phase may be more than 24 hours.
- However, until the very last stage of shock, a patient appears conscious and alert. If the patient is not closely monitored early shock could be missed.

Annexure: Critical monitoring chart

Monitoring of a patient with evidence of compensated shock /decompensated shock.

- Vital parameters and CRFT should be checked every 15 minutes until the patient are haemodynamically stable.
- During intense fluid resuscitation, inpatient Hct should be checked immediately before and 10-15 minutes after each fluid bolus and at least two to three hourly.
- If the shock is prolonged (not responding to initial fluid bolus) an indwelling urinary catheter should be inserted and urine output should be measured hourly. UOP of 0.5 ml to 1 ml/kg body weight / hour is adequate during this period. Overenthusiastic fluid replacement to achieve a higher UOP may lead to fluid overload.
- Liver profile, blood sugar, serum calcium, serum electrolytes, serum creatinine, clotting profile and venous blood gases and Lactate levels should be done in complicated cases such as prolonged shock, not responding to adequate fluid resuscitation, liver involvement and renal involvement.
- Once the patient is stabilized monitoring can be spaced out. Monitoring of vital parameters 2- 4 hourly and UOP every 4hourly would be adequate depending on the patient's haemodynamic status.

Monitoring in equilibrium phase

- In some patients, after the 48 hours of critical phase, symptoms and signs of recovery may not be seen for several hours.
- Their UOP may be marginal and Hct/PCV may fluctuate.
- In such patients' critical phase monitoring should be continued unless they show features of convalescence.

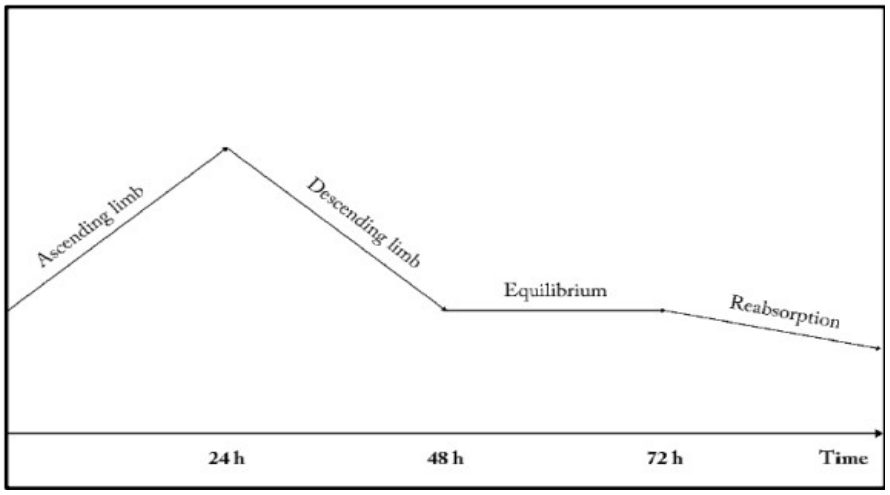


Figure 20: Equilibrium phase

Clinical Improvement Criteria

- Progressive waning of warning signs and general symptoms
- Stable vital signs
- Normal urine output (>0.5 – 1.5 mL/kg/ hr)
- Adequate oral intake
- Increase in appetite

Monitoring of a patient during convalescent phase.

- Bradycardia is an expected finding in the convalescent period, which is usually asymptomatic and transient.
- High urine output is observed in most patient.
- However, some patients may develop fluid overload during the convalescent phase. Therefore, it is important to observe for symptoms and signs of fluid overload.
- Rising respiratory rate is the most important sign for early detection of fluid overload.
- Continuous monitoring of vital signs and maintenance of intake and output chart is necessary for patients with fluid overload.
- However, the frequency of vital sign monitoring can be reduced if the patient is stable. (Initially 3-4 hours later 6-12 hours)
- Hct monitoring can be reduced to daily and when platelet count is rising, Hct monitoring can be stopped in stable patients

5.4 Fluid management in dengue:

Fluid replacement is the most important measure in the management of DF/DHF. Adequate fluid replacement is essential to avoid dehydration during the febrile phase, and to avoid shock due to significant plasma leakage in the critical phase. Careful fluid replacement during the equilibrium phase and convalescence/ reabsorption phase in a DHF patient is important to avoid fluid overload.

5.4.1 Febrile phase:

- During febrile phase, intake of adequate amount of fluid is important to avoid dehydration.
- The fluid intake should be adequate to replace the urine output and insensible loss. Additional losses such as vomiting and diarrhoea should be replaced according to the volume loss. If the patient is dehydrated on admission, it should be corrected accordingly.
- For all hospitalized patient it is not mandatory to have IV access. Intravenous line should be judicious according to need of the patient. In case of IV access, it is better by inserting preferably a large bore (18 G - Green) cannula.
- Consider IV fluids for patients who are unable to take adequate volume of oral fluid, or patients with diarrhoea or vomiting.
- Oral fluids should consist of electrolyte solutions such as coconut water, other fruit juices, oral rehydration fluid and soup. Drinking plain water should be discouraged.
- The recommended solutions for IV fluid therapy are 0.9% saline (Normal saline) or Hartmann's solution. The total amount of fluid (both IV and oral) should be limited to 2400 ml for 24 hours for an average adult (2 ml/Kg/hr up to a maximum of 50 Kg of weight).
- However, if there is vomiting or diarrhoea this amount should be increased, and dehydration should be corrected. State of hydration should be monitored by urinary output.

5.4.2 Critical Phase:

It is extremely important to replace fluid accurately during the critical phase. With plasma leakage, there is an additional loss of fluid from the intravascular compartment (in addition to urine and insensible loss). Systemic review and meta-analysis reveal crystalloid is first line and colloid as rescue therapy. (Level 1)

Calculation of the fluid quota for the critical phase:

- Fluid quota is **only a guide** for the management of dengue patients during the critical period of DHF.
- Patients managed using fluid within this safe quota, are less likely to develop fluid overload.
- The amount of fluid recommended during the entire critical phase (irrespective of its length) should be **Maintenance + 5% of weight (50ml/kg)**.
- All patients will not need the full quota of M+ 5% fluid, and many may need less than this, as the rate, peak and duration of leaking are variable from patient to patient. Some patients may need fluid above the calculated fluid quota to maintain vital parameters.

Calculations for normal maintenance of intravenous fluid infusion per hour:

(Equivalent to Halliday-Segar formula)

4 mL/kg/h for first 10kg body weight
+2 ml/kg/h for next 10kg body weight
+1 ml/kg/h for subsequent kg body weight

*For overweight/obese patients calculate normal maintenance fluid based on ideal body weight

Ideal bodyweight can be estimated based on the following formula
Female: 45.5 kg + 0.91 (height -152.4)cm
Male: 50.0 kg + 0.91(height-152.4) cm

Example of fluid calculation for a 50 kg person

For the 1st 10 kg - 100 ml/kg = 1000 ml

For the 2nd 10 kg - 50 ml/kg = 500 ml

From 20 kg and above up to 50 kg -20 ml/kg = 600 ml

5% deficit is calculated as 50 ml/kg up to 50 kg = 2500 ml

Total = 4600 ml

If the body weight is less than 50 kg, calculation should be done according to the ideal body weight or actual body weight whichever is less.

Try to assess the amount of fluid patient got before reaching your hospital.

Note: Therefore, the maximum usual fluid requirement for an average adult for the entire critical phase (48 hours) is 4600 ml. This is only a guide, and this volume is calculated considering a patient with fluid leakage amounting to moderate dehydration. Some patients might need a higher amount of fluid, especially if they develop shock.

Height in Inch	Estimated body weight (Kg) in male	Estimated body weight (Kg) in female
5 feet	50	45.5
5 feet 1 inch	52.3	47.8
5 feet 2 inch	54.6	50.1
5 feet 3 inch	56.9	52.4
5 feet 4 inch	59.2	54.7
5 feet 5 inch	61.5	57
5 feet 6 inch	63.8	59.3
5 feet 7 inch	66.1	61.6
5 feet 8 inch	68.4	63.9
5 feet 9 inch	70.7	66.2
5 feet 10 inch	73	68.5
5 feet 11 inch	75.3	70.8
6 feet	77.6	73.1

Table 8: Estimated ideal body weight for overweight or obese person.

Ideal wt (kg)	Maintenance(ml)	M+5% deficit (ml)	Ideal body wt (kg)	Maintenance (ml)	M+5% deficit (ml)
5	500	750	**35**	1800	3550
10	1000	1500	**40**	1900	3900
15	1250	2000	**45**	2000	4250
20	1500	2500	**50**	2100	4600
25	1600	2850	**55**	2200	4950
30	1700	3200	**60**	2300	5300

Table 9: Requirement of fluid based on ideal body weight

Fluid quota is aimed at giving just an adequate amount of fluid to maintain perfusion to vital organs without causing fluid overload. Once the fluid quota is exceeded the chances of fluid overload are high.

Guide to the rate of fluid administration:

- The fluid rate should be adjusted according to the rate of leaking**.**

5.4.3 Types of fluids required for Intravenous therapy:

The following fluids are recommended both crystalloids and colloids Crystalloids

- 0.9% NaCl (isotonic normal saline solution) (0.9% NS) (Preferable)
- 0.45% half strength normal saline solution (0.45% NS) (For children <6 months)
- 5% dextrose in lactated Ringer's solution (5% DRL)
- 5% dextrose in acetated Ringer's solution (5% DRA)
- Hartman solution (Preferable)

Colloids:

- Dextran 40
- 6% Hydroxy Ethyl Starch (level 6)
- Human Albumin
- Plasma
- Hemaceel (3.5% solution of urea cross-linked polygeline in a mixed salt solution)
- Blood & Blood Components

Ringer's lactate is a safe, effective, and inexpensive alternative in initial resuscitation of patients with moderate shock. In patients with shock, dextran and starch perform similarly although repeated dextran 40 is associated with more hypersensitivity reactions.

Colloids should be used:

- In patients whose shock does not respond to two boluses of crystalloids with rising Hct or still high Hct
- In patients who are being treated for shock, have high Hct and whose fluid quota (M+5%) is nearing completion
- In patients who present in shock and fluid overload
- Patients who need more fluids in the latter part of the critical phase and when their fluid quota is nearly exceeding.

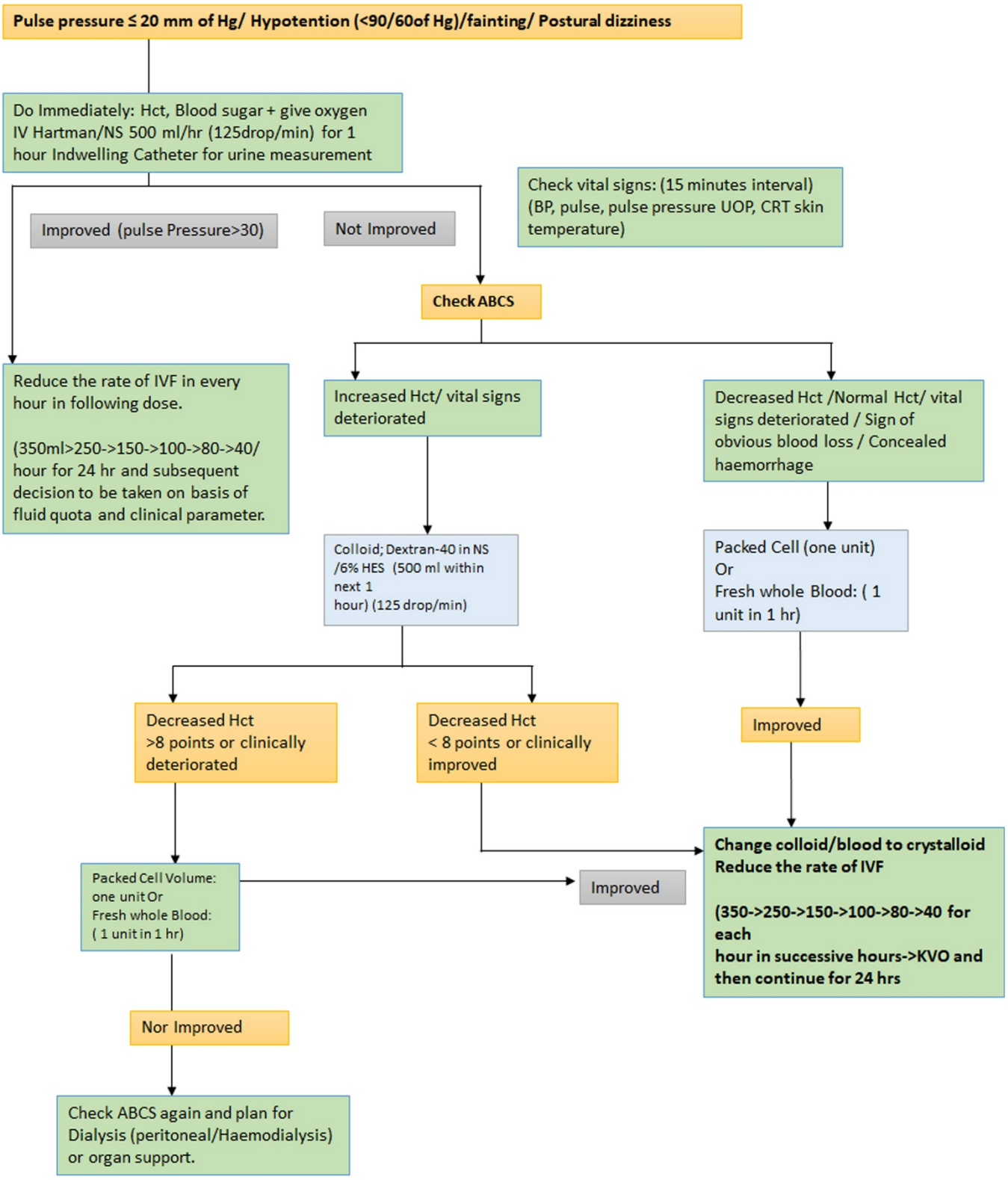
5.4.4 Non shock critical stage fluid management:

- The admitted patient should be started with recommended fluid at a rate of 40ml/hr (12 d/min). If patient's vital signs are stable, then the same rate can be maintained for a period of 48 hours. Remaining fluid as per weight to be taken orally not exceeding 4600ml in 50 kg patient in 48 hours.
- Patient should be monitored every 1 hour with special attention to vital signs, urine output, respiratory signs and haematocrit value.
- If patient develops unstable vital signs and/or inadequate urine output, patient should be shifted to compensated/decompensated dengue shock treatment protocol. (Flow chart …)
- Reassess the clinical status, repeat the haematocrit and review fluid infusion rates accordingly.
- Patients with warning signs should be monitored by health-care providers until the period of risk is over. A detailed fluid balance should be maintained.

Note:

- Crystalloid 500 ml: Drop Hct 1-2 points. If drops >3 points think about bleeding. Need blood transfusion.
- Dextran 500 ml: Drop Hct 8-10 points. If drops more, think about bleeding. Need blood transfusion.
- Blood transfusion: 1-unit BT /1 unit packed cell transfusion increase Hct 3-5 points.
- Before starting colloid, blood grouping and cross matching to be done as interferes with grouping and cross matching.
- Every secondary and tertiary care hospital should have capacity to supply blood and blood product during dengue outbreak.
- Nursing stuff should be adequately trained for monitoring dengue patients.

Fluid management in compensated dengue shock



Dextran 40 in NS: Dextran 40 in normal saline, 6% HES: 6% hydroxy ethyl starch.

Figure 21: Flow diagram for fluid therapy for compensated shock.

Flow Diagram for Profound Shock / Decompensated Shock

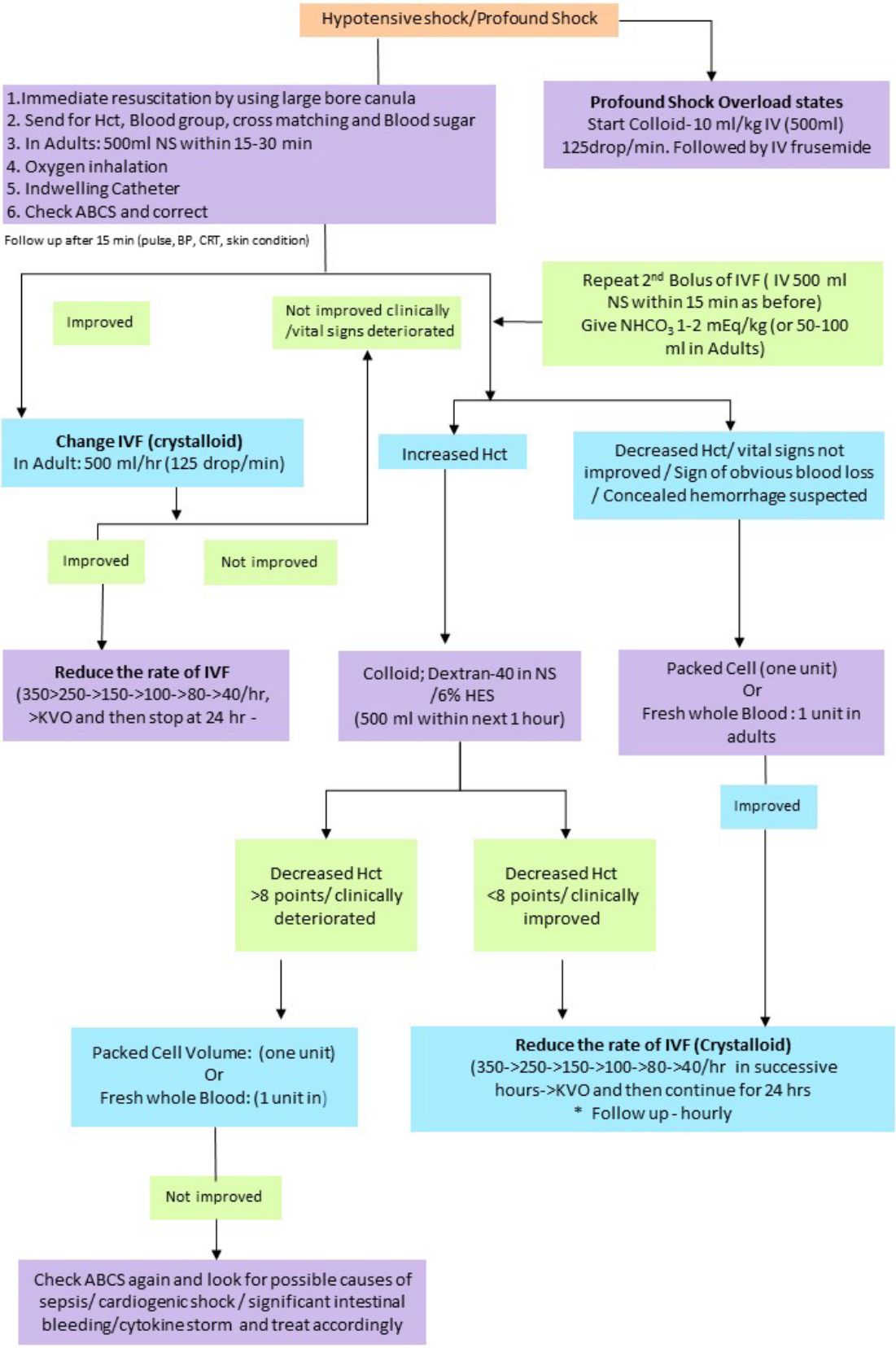


Figure 22: Flow diagram of fluid therapy for decompensated shock

5.4.5 Patients not responding to fluid resuscitation (or with refractory shock)

If the patient is not responding to two boluses of crystalloid, contributory causes for shock other than plasma leakage should be considered.

These are,

- Acidosis -check venous blood gas including serum lactate
- Bleeding -check Hct
- Calcium- Check serum calcium and electrolytes (sodium and potassium)
- Sugar -check random capillary blood sugar.

5.4.6 Management of diarrhoea in dengue patients:

Dengue patients frequently have diarrhea and require proper management.

- Replacement fluid would be cholera saline
- Beside general management of cholera/ diarrhoea patient will get 200-300 ml cholera saline in bolus after each purging / 250-500 ml ORS after each purging.
- Monitoring of urine output must be observed
- Don't use any antibiotic/ anti-diarrhoeal medication.

5.4.7 Fluid Overloaded Patient:

Some degree of fluid overload may develop in patients with severe plasma leakage. The skill is in giving them just enough intravenous fluid to maintain adequate perfusion and at the same time avoiding fluid overload.

Causes of fluid overload:

- Excessive intravenous fluids during the critical phase.
- Incorrect use of hypotonic crystalloid solutions e.g. 0.45% sodium chloride solutions.
- Inappropriate use of large volumes of intravenous fluids for correction of shock in patients having concealed bleeding.
- Inappropriate use of crystalloid solution in place of colloid
- Inappropriate transfusion of fresh-frozen plasma, platelet concentrates and cryoprecipitates.
- Prolonged intravenous fluid therapy, i.e., continuation of intravenous fluids after critical phase.
- Co-morbid conditions such as congenital or ischaemic heart disease, heart failure, chronic lung and renal diseases.

Clinical features of fluid overload:

- Rapid breathing / respiratory distress
- Suprasternal in-drawing and intercostal recession (in children)
- Basal crepitations
- Increased jugular venous pressure (JVP)
- Puffy face & leg oedema.

Management of fluid overload:

- Review the total intravenous fluid therapy, clinical course, check and correct for ABCS.
- Stop all IV fluid if patient is not in shock
- Switch from crystalloid to colloid solutions as bolus fluids if the patient is in shock
- Dextran 40 is effective as 10 ml/kg bolus infusions, but the dose is restricted to 30 ml/kg/day because of its renal effects.
- Intravenous frusemide should be administered if the patient has stable vital signs.
- When the blood pressure is stable, usually within 10 to 30 minutes of administer IV 1 mg/kg/dose of frusemide and continue with infusion, dextran infusion until completion.
- Intravenous fluid should be reduced to as low as 1 ml/kg/hr until when haematocrit decreases to baseline or below (with clinical improvement).

Management of fluid overload

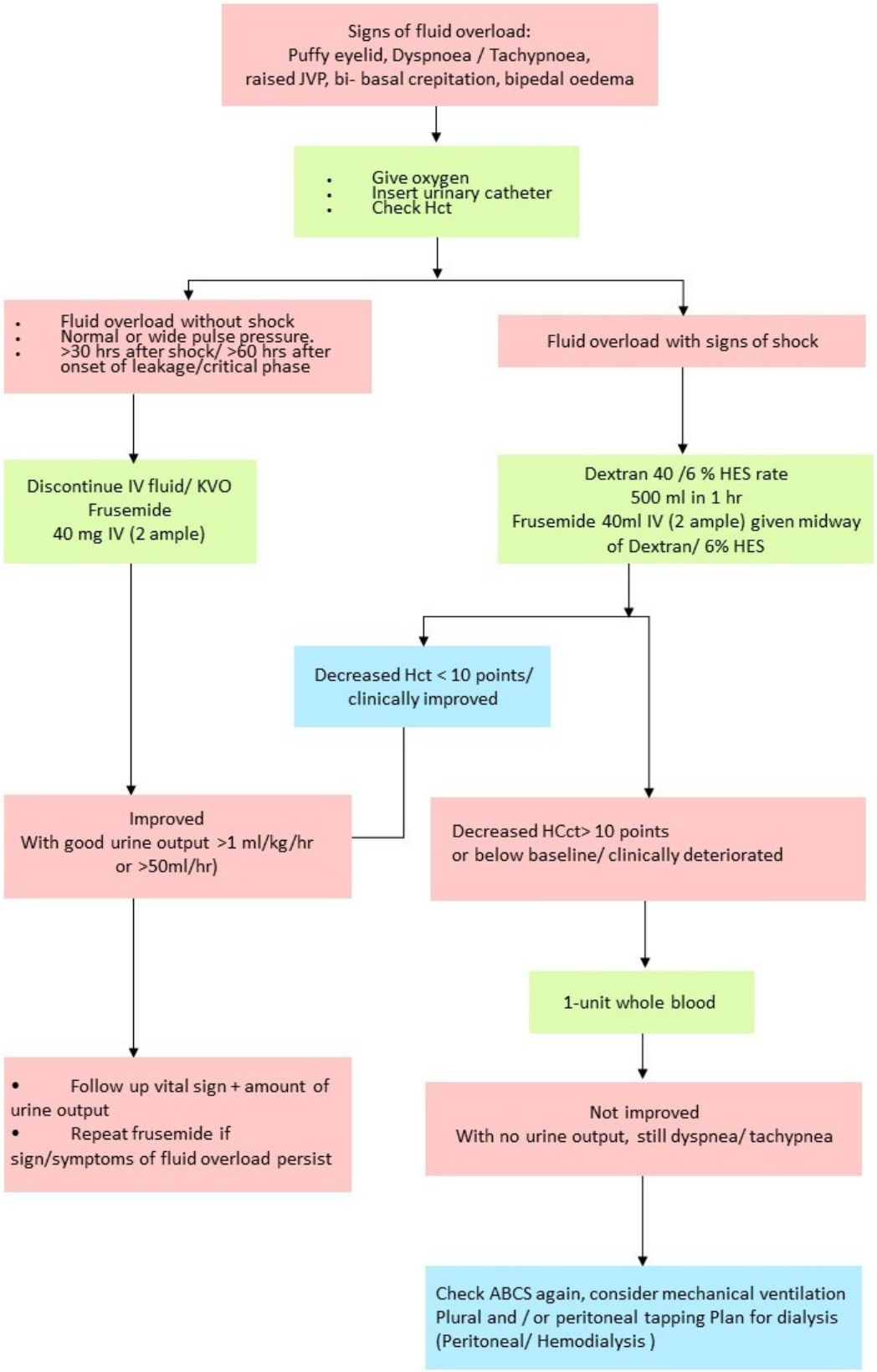


Figure 23: Flow diagram for the Management of Fluid overload

The following points should be noted:

- These patients should have a urinary catheter to monitor hourly urine output
- Intravenous Frusemide should be administered during dextran infusion because the hyper tonic nature of dextran will maintain the intra vascular volume while furosemide depletes in the intravascular compartment. After administration of frusemide, the vital signs should be monitored every 15 to 30 minutes interval for one hour to note its effects.
- In cases with no response to furosemide (no urine obtained), repeated doses of furosemide and doubling of the dose are recommended. If oliguric renal failure is established, renal replacement therapy is to be done as soon as possible. These cases have poor prognosis.
- If there is no urine output in response to furosemide, check the intravascular volume status (CVP or lactate). If this is adequate, pre-renal failure is excluded, implying that the patient is in an acute kidney injury state. These patients may require ICU/dialysis support soon. If the intravascular volume is inadequate or the blood pressure is unstable, check the ABCS and other electrolyte imbalances
- Pleural and/or abdominal tapping may be indicated and can be life-saving in cases with severe respiratory distress and failure of the above management. This has to be done with extreme caution because traumatic bleeding is the most serious complication and can be detrimental. Discussions and explanations about the complications and the prognosis with families are mandatory before performing this procedure.

5.5 Treatment of bleeding:

Risk factor for overt or covert bleeding

- Profound/prolonged/refractory shock
- Hypotensive shock and multi-organ failure
- Pre-existing peptic ulcer disease
- Any form of trauma, including intramuscular injection
- Patient on-steroidal or anti-inflammatory agents
- Anticoagulant therapy/anti platelet drug.

Severe bleeding should be suspected in the following situations:

- Unstable haemodynamic status, regardless of the haematocrit level.
- Decrease in haematocrit after bolus of fluid resuscitation unstable haemodynamic status.
- Refractory shock that fails to respond to consecutive fluid resuscitation of 40– 60 ml/kg.
- Hypotensive shock with inappropriately low/normal haematocrit.
- Persistent or worsening metabolic acidosis.

Treatment of bleeding are as follows:

- If possible, attempts should be made to stop bleeding if the source of bleeding is identified e.g. severe epistaxis may be controlled by nasal adrenaline packing.
- Give aliquots of one unit fresh -packed red cells or one unit whole blood (FWB) at an appropriate rate and observe the clinical response.
- It is important that fresh whole blood or fresh red cells are given.
- Oxygen inhalation-2-4 L/min
- Consider repeating the blood transfusion if there is further overt blood loss or no appropriate rise in haematocrit after blood transfusion in an unstable patient.
- There is no evidence that supports the practice of transfusing platelet concentratesand/or fresh-frozen plasma for severe bleeding in dengue.
- Transfusions of platelet concentrates and fresh frozen plasma in dengue were not able to sustain the platelet counts and coagulation profile. Instead, in the case of a massive bleeding, they often exacerbate the fluid overload.
- In certain situations, such as obstetrical deliveries or other surgeries, transfusions of platelet concentrate with or without fresh blood should be considered in anticipation of severe bleeding.
- In gastrointestinal bleeding, H-2 antagonist and proton pump inhibitors have been used, but their efficacy have not been studied.
- Great care should be taken when inserting a nasogastric tube or bladder catheters which may cause severe haemorrhage. A lubricated orogastric tube may minimize the trauma during insertion. Insertion of central venous catheters should be done with ultra-sound guidance or by an experienced person.

5.6 Indications for Platelet Concentrate:

It has been observed that there is very limited role of platelet transfusion. In most of the situation fresh whole blood transfusion is suffice. However, it may be required in some special situation. The indication of which may be as follows:

1. Very Severe thrombocytopenia who need urgent surgery
2. Clinical judgement of the treating physician

5.7 Calcium Replacement:

Hypocalcaemia has been demonstrated in dengue infection and often under-recognized. Hypocalcaemia maybe more pronounced in severe/ critically ill dengue. IV calcium gluconate may be used empirically, in the following situations

- Patients with DHF where blood pressure not responding to two boluses of crystalloids
- Any patient with shock
- DHF/ DF patients receiving > 2 unit of PRC
- Patients with dengue myocarditis
- Other clinical conditions - As decided by the treating clinician e.g., Inadequate clinical improvement despite adequate fluid resuscitations

Treatment is with 10% calcium gluconate 10 ml over 10 minutes. This may be continued six hourly for 24 hours.

5.8 Glucose control:

- Hyperglycaemia and hypoglycaemia may occur in the same patient at different times during the critical phase.
- Hyperglycaemia is associated with increased morbidity and mortality in critically ill adult and paediatric patients.
- Hypoglycaemia may cause seizures, mental confusion and unexplained tachycardia.
- Most cases of hyperglycaemia will resolve with appropriate (isotonic, non-glucose) and adequate fluid resuscitation.
- In infants and children, blood glucose should be monitored frequently during the critical phase and into the recovery phase if the oral intake is still reduced.
- However, if hyperglycemia is persistent, undiagnosed diabetes mellitus or impairedglucose tolerance should be considered and intravenous insulin therapy initiated.
- Hypoglycaemia should be treated as an emergency with 0.1–0.5g/kg of glucose, rather than with a glucose-containing resuscitation fluid.
- Frequent glucose monitoring should be carried out and euglycaemia should then be maintained with a fixed rate of glucose-isotonic solution and external feeding if possible.

5.9 Electrolyte and acid-base imbalances:

- Hyponatraemia is a common observation in severe dengue
- The use of isotonic solutions for resuscitation will prevent and correct this condition.
- Hyperkalaemia is observed in association with severe metabolic acidosis or acute renal injury.
- Appropriate volume resuscitation will reverse the metabolic acidosis and the associated hyperkalaemia.
- Life-threatening hyperkalaemia, in the setting of acute renal failure should be managed with Resonium. A infusions of calcium gluconate and/or insulin- dextrose.
- Renal support therapy may have to be considered.
- Hypokalaemia is often associated with gastrointestinal fluid losses and the stress-induced hypercortisol state;
- It should be corrected with potassium supplements in the parenteral fluids.
- Serum calcium levels should be monitored and corrected when large quantities of blood have been transfused or if sodium bicarbonate has been used.

Metabolic acidosis:

- Compensated metabolic acidosis is an early sign of hypovolaemia and shock.
- Lactic acidosis due to tissue hypoxia and hypoperfusion is the most common cause of metabolic acidosis in dengue shock.
- Correction of shock and adequate fluid replacement will correct the metabolic acidosis.
- If metabolic acidosis remains uncorrected by this strategy, one should suspect severe bleeding and check the haematocrit. Transfuse fresh whole blood or fresh packed red cells urgently.
- Sodium bicarbonate for metabolic acidosis caused by tissue hypoxia is not
- recommended for pH ≥ 7.10. Bicarbonate therapy is associated with sodium and fluid overload, an increase in lactate and pCO2 and a decrease in serum ionized calcium. A left shift in the oxy– haemoglobin dissociation curve may aggravate the tissue hypoxia.
- Hyperchloraemia, caused by the administration of large volumes of 0.9% sodium chloride solution (chloride concentration of 154 mmol/L), may cause metabolic acidosis with normal lactate levels.
- If serum chloride levels increase, use Hartmann's solution or Ringer's lactate as crystalloid. These do not increase the lactic acidosis.

5.10 Signs of recovery:

- Stable pulse, blood pressure and breathing rate.
- Normal temperature.
- No evidence of external or internal bleeding.
- Return of appetite.
- No vomiting, no abdominal pain.
- Good urinary output.
- Stable haematocrit at baseline level.
- Convalescent confluent petechiae rash or itching, especially on the extremities.

5.11 Discharge Criteria:

- No fever for at least 24 hours without the usage of antipyretic drugs
- At least two days have lapsed after recovery from shock
- Good general condition with improving appetite
- Normal Hct at baseline value or around 38 - 40 % when baseline value is not known
- No distress from pleural effusions
- No ascites and other complications
- Platelet count has risen above 50,000 /mm3.

5.12 Dengue with Complications:

- Dengue encephalopathy
- Dengue with Carditis
- Hemophagocytic Lymphohistiocytosis (HLS)

Dengue encephalopathy:

- Some DF/DHF patients present unusual manifestations with signs and symptoms of central nervous system (CNS) involvement, such as convulsion and/or coma. This has generally been shown to be encephalopathy, not encephalitis, which may be a result of intracranial haemorrhage or occlusion associated with DIC or hyponatremia.
- Most of the patients with encephalopathy are reported to have hepatic encephalopathy. The principal treatment of encephalopathy is to prevent the increase of intracranial pressure (ICP). Radiological imaging of the brain (CT scan or MRI) is recommended if available to rule out intracranial haemorrhage.

Recommendations for supportive therapy for this condition:

- Maintain adequate airway oxygenation with oxygen therapy.
- Maintain ICP by the following measures:
- Give minimal IV fluid to maintain adequate intravascular volume; ideallythe total IV fluid should not be >80% fluid maintenance.
- Switch to colloidal solution earlier if haematocrit continues to rise and a large volume of IV is needed in cases with severe plasma leakage.
- Administer a diuretic if indicated in cases with signs and symptoms of fluid overload.
    - Positioning of the patient must be with the head up by 30 degrees.
    - Early intubation to avoid hypercarbia and to protect the airway.
    - Intravenous mannitol
    - Consider steroid to reduce ICP. Dexamethasone 0.15 mg/kg/dose IV tube administered every 6–8 hours.

- Decrease ammonia production by giving lactulose 5–10 ml every six hours for induction of osmotic diarrhoea. Local antibiotic gets rid of bowel flora; it is not necessary if systemic antibiotics are given.
- Maintain blood sugar level at 80–100 mg/dl per cent. Recommend glucose infusion rate is anywhere between 4–6 mg/kg/hour.
- Correct acid-base and electrolyte imbalance, e.g. correct hypo/hypernatremia, hypo/ hyperkalemia, hypocalcemia and acidosis. Vitamin K1 IV administration; 3mg for <1-year-old, 5 mg for <5-year old and 10 mg for>5-year-old and adult patients.
- Anticonvulsants should be given for control of seizures: phenobarbital, dilantin and diazepam IV as indicated.
- Transfuse blood, preferably freshly packed red cells, as indicated. Other blood components such as as platelets and fresh frozen plasma may not be given becausethe fluid overload may cause increased ICP.
- Empiric antibiotic therapy may be indicated if there are suspected superimposed bacterial infections.
- H2-blockers or proton pump inhibitor may be given to alleviate gastrointestinal bleeding.
- Consider plasmapheresis or haemodialysis or renal replacement therapy in cases with clinical deterioration.

Dengue Myocarditis:

Dengue myocarditis is considered an uncommon complication of dengue, although its reported incidence is likely an underestimation. In general, most cases of dengue myocarditis are self-limited, with only a minority at risk of progressing to heart failure.
In dengue myocarditis, the inflammatory process can affect the myocytes, the vascular structures, the conduction system, the autonomic nerves, and the interstitium, and it is not infrequent that the pericardium is affected by contiguity. Myocardial damage is likely the combined effect of a direct viral attack and an added immune-mediated lesion.

The clinical manifestations of dengue myocarditis range from silent forms to symptoms of chest pain, dyspnea, heart failure, pulmonary edema, or cardiogenic shock. Dengue myocarditis can even imitate acute myocardial infarction. Arrhythmias including sinus tachycardia, ventricular arrhythmias, supraventricular arrhythmias such as atrial fibrillation, and/or varying degrees of atrioventricular block can be detected.

Echocardiography usually reveals structural and functional abnormalities such as dilation of the cardiac chambers, systolic and diastolic dysfunction, pericardial effusion, and valvular insufficiencies. In addition, cardiac biomarkers, including troponins and NT-proBNP, are often elevated. Cardiac MRIs have become a useful non-invasive method due to their unique ability to characterize tissue in a multiparametric manner. Endomyocardial biopsy remains the gold standard for establishing a definitive diagnosis of myocarditis. But this method has several limitations.

There is no specific treatment for dengue induced myocarditis. Management includes rest, adequate hydration, and seeking medical advice for complications. Presence of myocardial dysfunction should not be a hindrance to fluid management in dengue. Myocardial dysfunction can be seen commonly in patients who are in prolonged shock due to metabolic acidosis. Hypocalcaemia (which is a common finding in DHF patients with moderate to large pleural effusion / ascites) may be a contributory factor. Therefore, empirical treatment with calcium is justifiable in patients with large pleural effusion/ascites. Myocarditis is an uncommon finding in dengue and is very unlikely to cause death in a patient with DHF. However, such a patient could easily develop pulmonary oedema due to fluid overload.

Hemophagocytic lymphohistiocytosis (HLH):

HLH is a rare, aggressive and life-threatening syndrome induced by aberrantly activated macrophages and cytotoxic T cells which can occur rarely in dengue patients.

When to suspect HLH in dengue:

- Persistent fever after 6 days and
- Worsening cytopaenia after 6 days of fever (throbocytopaenia/, leucopaenia/ anaemia) together with clinical deterioration of the patient.

In addition, such patients can have:

a) Organomegaly (splenomegaly is very common. May have hepatomegaly also).
b) Lymphadenopathy
c) Neurologic dysfunction (such as encephalitis, seizures, or coma), oedema, dermatologic manifestations, and stigmata of liver dysfunction or coagulopathy (such as jaundice or bruising)

The diagnosis of HLH can be established if either A or B is fulfilled: (HLH-2004):

A. A molecular diagnosis consistent with HLH
B. Any 5 of the 8 following clinical and laboratory criteria for HLH:
    a) Fever >38.5° C
    b) Splenomegaly
    c) Cytopenia (affecting ≥2 of 3 lineages in peripheral blood):
        - Hemoglobin <9 g/dL (in infants <4 weeks: Hb <100 g/L)
        - Platelets $<100\times10^9$/L
        - Neutrophils $<1.0\times10^9$/L
    a) Hypertriglyceridemia and/or hypofibrinogenemia: fasting triglycerides >3.0 mmol/L (>265 mg/dL) or fibrinogen ≤1.5 g/L
    b) Hemophagocytosis in bone marrow, spleen, liver, lymph nodes, or other tissues
    c) Low or absent natural killer (NK) cell activity
    d) Serum ferritin concentration ≥500 µg/L
    e) Soluble CD25 (soluble IL-2 receptor) ≥2400 U/mL

Other features supporting an HLH diagnosis that are not part of the above HLH-2004 criteria include hyperbilirubinemia, hepatomegaly, hypertransaminasemia (present in the vast majority of patients with HLH) elevated lactate dehydrogenase and d-dimer levels.

Management:

HLH has a high mortality rate especially if there is a delay in commencing treatment. Therefore, prompt treatment is critical. On occasions, HLH may be strongly considered, and HLH-directed therapy may be initiated, even though all 5 criteria are not fulfilled Mainstay of treatment is dexamethasone, which is initially given IV 10 mg/m^2/d. Once the patient improves, this can be changed to oral and tailed off. In addition, IV immunoglobulin 0.75 g/Kg stat followed by 0.4g/Kg given for 3 days can be considered. Etoposide is suggested as a rescue therapy. In addition, giving broad spectrum antibiotics and adequate fluid therapy is important in these patients.

5.13 Some Important Notes:

No existing antivirals are effective in dengue fever.

Role of steroid:

Basis of DHF pathogenesis is hypothesized to be immunologic that is tempting for immunomodulatory drugs for therapy most common of which is steroid. Cochrane reviews and other studies have found the evidence on corticosteroids for treating dengue to be inconclusive and of low to very low quality. (Level1).

But steroid has been used in Dengue Encephalopathy (Level 7) and Hemophagocytic Syndrome (empirically with anecdotal benefits.

There has been used of different formulation of steroids in severe dengue with refractory shock case in different regions of globe, but there is lack of sufficient conclusive evidence.

Well-designed Randomized Control Trial for steroids in severe dengue should be completed before strong recommendation can be solicited.

Special Concerns:

Older patients, particularly those with congestive heart failure, must not be given excessive amounts of intravenous fluids.

Rare cases of vertical dengue transmission have been reported. Dengue should be suspected in pregnant patients with compatible clinical features. The potential for a neonate to be born with signs and symptoms of dengue fever should be anticipated.

Pitfalls:

- Failures to suspect, identify, and treat other possible diseases such as meningitis or malaria.
- Failure to admit patients with signs and symptoms of intravascular volume loss for intravenous hydration.
- Failure to administer appropriate fluids to patients with dengue haemorrhagic fever or dengue shock syndrome (moderate and severe) in proper rate.
- Failure to refer or transfer potentially critical or critical patients to better facility in time.
- Failure to notify public health authorities about suspected cases of dengue infection.

Check list:

- Cases of DHF should be observed every hour.
- Serial platelet and Hct determinations for drop in platelets and rise in Hct are essential for early diagnosis of DHF
- Timely intravenous therapy with isotonic crystalloid solution may prevent shock and or lessen the severity. Be careful about the temperature of fluid to avoid chills and rigors.
- If patient's condition becomes worse despite giving 10 ml/kg/hour in children (500 ml in adult/one hour), replace crystalloid solution with colloid solution such as Dextran or plasma. As soon as improvement occurs replace with crystalloid and reduce the speed from 10 ml to 7 ml, then 5 ml, then 3ml and finally to 1.5 ml/kg in child (350, 250, 150, 80 then 40ml/hour in adult).
- If Hct falls, give blood transfusion 10 ml/kg and then give crystalloid IV fluids at the rate of 10 ml/kg/hour.
- In case of severe bleeding, give blood transfusion about 10 ml/kg over 1 - 2 hours. Then give crystalloid at 10 ml/kg/hour for a short time (30-60 minutes) and later reduce the speed.
- In case of shock, give oxygen.

- For correction of acidosis, use sodium bicarbonate. Acidosis should be partially corrected if base deficit is more than 6 mmol/L. Half of the calculated based deficit should be administered as 1-2 mmol/kg of Sodibicarbonate IV over 20 minutes. Available Sodibicarbonate solution in Bangladesh is of the strength 7.5%
- i.e. 1 ml contains 2 mmol/ml. So, 50 - 100 ml of Sodibicarbonate is to be added to make up to one liter of IV fluid of glucose containing crystalloid.
- Check for any concomitant other medical or surgical condition and or any maintenance therapy.

Don't

- Do not give aspirin or NSAID for the treatment of fever.
- Avoid giving blood transfusion or platelet concentrate unless there is hemorrhage and bleeding, fall in Hct or severe bleeding.
- Do not use antibiotics per see for dengue syndromes.
- Do not change the infusion rate of fluid rapidly or abruptly i.e., avoid rapidly increasing or rapidly slowing the infusion rate of fluids.
- Insertion of nasogastric tube to determine concealed bleeding or to stop bleeding (by cold lavage) is not recommended since it is hazardous.
- Avoid IM injections.
- Avoid tooth brushing in presence of gum bleeding.

Good Medical Practice for IV Therapy:

- Always collect and check necessary appliances before proceeding to IV puncture.
- Use gloves to protect yourself and mask to protect the patient. Wash hands with antiseptic before handling cannula/needle. Always use disposable items. Be careful about needle stick injury.
- For IV choose a vein at a site having the following criteria: Distal, relatively less mobile and inactive, away from joint with overlying healthy skin and after shaving hairs. If necessary, immobilize the part with sprint. Keep proximal sites reserve for future puncture if necessary.
- Preferably use cannula having wider bore (18G or wider), which may allow high flow rate and blood transfusion if necessity arises for avoiding further puncture. Properly fix the cannula with adhesive tape. Put date and time of infusion/transfusion beginning on bag and on adhesive tape.
- Insert the cannula or needle along the lengths of vein appropriately to avoid extravasation and check the site frequently for it. Avoid multiple punctures.
- Don't keep the cannula/needle in a same site for more than 48 hours to avoid phlebitis.
- If extravasation occurs immediately remove the cannula/needle and keep the part elevated.
- Always check the fluid bag for deposits, puncture, leaking, proper seals in the port, dirt and labels. In such cases discard the bag. Similarly check the infusion/transfusion sets and cannula. Never reuse any disposables and remaining fluid in bag.
- For high flow rate never use cold fluid to avoid chills and discomfort. Warm the fluid near to body temperature by placing on the cover of the sterilizer and not immersing in that.
- Always dispose the disposables and sharps in a bin to be managed properly.
- Hang the fluid bag at appropriate height and check for proper fluid flow.

Dengue in Children

Chapter-6

6.1 Introduction:

Dengue can become life-threatening if not managed appropriately, particularly in children. Paediatric patients often present with atypical symptoms compared to adults, and fluid management requires special considerations due to differences in physiology. Given the complexity of dengue and these Paediatric-specific challenges, effective management hinges on early recognition of clinical features across different phases, enabling a rational approach to treatment and favorable clinical outcomes.

Situation analysis:

Current situation of Dengue in Bangladesh is worsening specially in Dhaka and other urban areas. As we know, no age is immune to Dengue and current literature showed there is significant increase in the dengue infection over the last few years (according to the national data). In Bangladesh, data from the Directorate General of Health Services (DGHS) reveals that approximately 17% of children (0-15 years) were affected by dengue in 2023. This proportion has risen to 19.3% in 2024

Why do children require special attention for dengue?

- Children have a higher body water content compared to adults, making them more prone to fluid shifts and dehydration during plasma leakage in severe dengue.
- Children have a smaller absolute blood volume (80 mL/kg) than adults, which means even minor plasma leakage or blood loss can lead to significant haemodynamic instability
- Paediatric patients are more prone to fluid overload due to their smaller cardiovascular and renal capacities, especially during the recovery phase when capillary permeability normalizes.
- Younger children may be unable to express symptoms (e.g., abdominal pain or fatigue) clearly, delaying recognition of warning signs.

6.2 Classification & clinical features:

The classifications and clinical features of dengue are thoroughly addressed in previous section (dengue in adult) of this guideline. Readers are encouraged to refer to that section for an in-depth understanding. Here, we will provide a concise overview of the key features. (page: 26)

Key Features of Dengue in Children

Dengue fever:

- High, continued fever for 2-7 days
- Headache
- Myalgia
- Arthralgia/ bone pain (break-bone fever)
- Rash
- GIT manifestation: Nausea, vomiting, diarrhea
- Haemorrhagic manifestations (mild, unusual haemorrhage)
- Leukopenia (WBC <5,000 cells/mm3)
- Platelet count ≤150,000 cells/mm3
- Rising HCT 5-10%

Diagnosis:

Tourniquet test positive + WBC ≤ 5.000 cells/cu.mm (positive predictive value = 83%)

Dengue Haemorrhagic Fever (DHF) Dengue shock syndrome (DSS) Evidence of Circulatory failure:

Readers are encouraged to refer to adult section for an in-depth understanding (page:33)

Note:

a) Abdominal symptoms (pain, nausea, vomiting, diarrhoea) are more common in children.
b) Co-infections are highly prevalent in paediatric populations; thus, the presence of symptoms such as cough and coryza does not exclude the diagnosis of dengue.
c) Negative tourniquet test doesn't exclude the diagnosis of dengue

High-risk factors for severe disease

- Infants
- Obesity or children with malnutrition
- Haemolytic diseases such as glucose-6-phosphatase dehydrogenase deficiency, thalassemia and other haemoglobinopathies
- Hypertension
- Congenital heart disease
- Chronic diseases such as diabetes and renal diseases, cardiovascular diseases chronic renal failure, and chronic liver disease. Chronic pulmonary diseases (Asthma & others)
- Patients on long term steroid or NSAID treatment

Warning signs: Readers are encouraged to refer to adult section for an in-depth understanding (page:28)

6.3 Investigations: Essential test:

6.1.1 Full Blood Count (FBC): Readers are encouraged to refer to adult section for an in-depth understanding (page: 38)

Note:
***When the baseline* Hct is not known, it is safe to assume that the baseline is around 35% and may be slightly lower in young children and infants, and higher in older children. The infants may have a lower Hct due to physiological and iron deficiency anaemia.**

6.3.2. Dengue antigen and antibody Tests: Readers are encouraged to refer to adult section for an in- depth understanding (page:39)

6.3.3. Serum AST (SGOT) and ALT (SGPT): Readers are encouraged to refer to adult section for an in-depth understanding (page:40)

6.3.4 Other tests:

Chest X-Ray: Pleural effusion on X-ray in dengue indicates fluid accumulation.

- Ultrasonography: To detect pleural effusions or ascites, Swollen pancreas, peripancreatic fluid collection etc. May be suggestive of acute pancreatitis. **Gallbladder wall thickening >5 mm considered to be a sign of severe dengue infection.**
- Urine R/M/E: Albuminuria/Hematuria may be present
- If high fever persists, ICT for malaria, microscopy for malaria, blood culture to exclude enteric fever or other sepsis. Procalcitonin or serum calprotectin can be done to detect bacterial infection

When available, point-of-care ultrasound (POCUS) is a valuable tool in the management of dengue in children. It is particularly useful for detecting plasma leakage, and guiding fluid therapy.

6.3.5 Additional test:

- Serum Creatinine/Blood urea nitrogen (BUN) may be elevated in prolonged shock.
- Serum Electrolyte: Hyponatremia is frequently observed in DHF/DSS
- VBG (venous blood gas analysis): Metabolic acidosis is frequently found in cases with prolonged shock.
- RBS may be low in DSS
- Serum calcium: Hypocalcaemia (corrected for hypoalbuminemia) has been observed in DHF.
- Serum Ferritin: Very high serum ferritin levels are seen in severe disease and in dengue-associated hemophagocytic lymphohistiocytosis (HLH)
- Assays of coagulation and fibrinolytic factors show reduction in DSS cases. Activated Partial thromboplastin time (aPPT) and prothrombin time (PT) are prolonged in about half and one third of DHF cases respectively. Thrombin time (TT) is also prolonged in severe cases.
- If abdominal pain present, serum lipase, amylase should be done to exclude pancreatitis.
- ECG, Echocardiography, Troponin I, CK-MB if myocarditis is suspected.
- CSF: In dengue encephalitis (Febrile convulsion is common in children. If the child previously diagnosed as a "febrile convulsion" please carefully evaluate the patient before performing lumber puncture.)

6.4 Outpatient Assessment and Management for Children:

- **IMCI -N corner** can be used as a **Fever Corner** – for febrile child
- Fever corner should consist of a **Triage Desk** where fever patients will be registered and assessed based on duration of Fever
- In the current hyper-endemic context of Bangladesh, dengue fever (DF and DHF) should be considered in any patient presenting with acute febrile illness. Clinical evaluation hinges on a thorough assessment of symptoms and signs.

Stepwise approach on Outpatient management on Dengue History

- Date of onset of fever/ illness
- Date and time of last episode of fever
- Appearance (Lethargic, restless)
- Feeding history including breast feeding status (amount, able to take oral food or not)
- Vomiting
- Warning signs
- Diarrhoea
- **Bleeding (menstrual history must not be missed when assessing adolescent girls)**
- seizure /dizziness
- Urine output (frequency, volume and time of last voiding)
- Other important relevant histories: drug history, comorbidities.

Physical examination

- Appearance
- **Hydration status (Use IMCI assessment criteria for dehydration)**
- Haemodynamic status (Pulse, BP, CRT)
- Tachypnoea/ acidotic breathing/ pleural effusion
- Abdominal tenderness/ hepatomegaly/ ascites
- Bleeding manifestation
- Nutritional status (Height, weight, MUAC, calculation of BMI)

Investigation

- Full Blood Count (FBC) and HCT
- NS-1
- **Dengue antibody: IgG, IgM (if available, when indicated)**
- SGPT/SGOT
- CRP

Patients at high risk for severe disease (warning signs and comorbid conditions) and its complications need admission. Child with adverse social conditions may require admission even if they do not meet the above criteria.

Patients with adverse social circumstances

- Parents has poor access to healthcare facilities
- Lack of transportation
- Unstable housing
- Extreme poverty
- Those with mental disabilities, for whom adequate fluid administration and regular follow-up cannot be ensured.
- Parents are also sick and cannot able to take care the child properly
- For any other condition (Parents knowledge, educational status, more than one child affected, etc.) that can hamper the proper take care of the dengue affected child.

For evaluation /home management/ hospital admission readers are encouraged to refer to adult section for an in-depth understanding (page: 46,47)

6.5 Home management of children:

- Patients without warning signs or coexisting conditions or social risk should get home based care.
- **Recommended measures in home management:**
- Comfortable clothing, and under a mosquito net
- Control of temperature by tepid sponging.
- Paracetamol 15mg/kg/dose can be given (Maximum 60mg/kg/24hrs in child)

Adequate hydration: Ensure adequate oral fluid intake. According to the World Health Organization (WHO) **and** various national guidelines**,** the recommended daily fluid intake at home for uncomplicated dengue is 50 mL/kg/day**.**

Age Group	Estimated Weight (kg)	Recommended Fluid Intake (mL/day)
Infants (0–12 months)	5–10 kg	250–700 mL
Toddlers (1–3 years)	10–14 kg	500–980 mL
Preschool (4–5 years)	15–18 kg	750–1260 mL
School-age (6–12 years)	19–30 kg	950–2100 mL
Adolescents (>12 years)	>30 kg	1500–2500 mL

- The fluid intake should mainly consist of oral rehydration solution (ORS), plain water, coconut water, clear soups, or fresh fruit juices.
- It is advisable to avoid red/ brown (i.e. dark) colored food (Red Dragon fruit, beet root)/ beverages to avoid confusion with blood-stained vomitus/ melaena)

- Avoid excessive sugary drinks, sodas, and caffeinated beverages**,** as they can worsen dehydration
- For children below 2 years of age, encourage frequent breastfeeding**.**
- Ensure adequate urine output. (Encourage to pass urine every 3-4 hours). It is useful to measure the urine output, if possible.
- Parents should be informed about warning sign.
- Anti-emetics and PPI if necessary.
- Avoid all NSAIDS and steroids (If the child already receiving steroid for Nephrotic syndrome or other disease continue that)
- Review daily with FBC. First FBC should be done at least at the beginning of the third day of fever/illness (preferably with SGOT and SGPT).
- These patients should be followed up until the patient become afebrile for 48 hours with stable clinical parameters. Usually, by seven days, most patients recover.
- If any indication for hospitalization appears within this follow up period, patient should get admitted to hospital.

6.6 Fluid Management Strategy:

- **Mild dehydration or fever**: Encourage small, frequent sips of fluids every **15–30 minutes**
- **Vomiting**: If the child vomits, pause for 30 minutes**,** then resume hydration with smaller volumes at a slower pace**.**
- **Monitoring**: Ensure the child passes light-colored urine at least 4–6 times a day.

Note: The settling of fever is not a sign of recovery, as some patients may begin plasma leakage around the time of defervescence

Indications for immediate return to hospital for hospitalization and review Advise patients to return to the hospital immediately, if they develop any of the following conditions**:**

- Clinical deterioration with settling of fever
- Inability to tolerate oral fluids
- Severe abdominal pain
- Behavior changes: confusion, restlessness, lethargy, irritability
- Bleeding tendency including inter-menstrual bleeding or menorrhagia
- Not passing urine for more than 6 hours
- Cold and clammy extremities.
- Any warning signs

If the patient need hospitalization, before admitting the patient from the OPD/emergency department to the in-patient department or transferring to another hospital, initial evaluation and specific measures must be implemented. (Read adult section section for details)

6.7 Inpatient Management of Dengue in Children:

Monitoring of Dengue patients during hospital stay:

- Every inpatient should be assessed thoroughly
- If the patient is clinically stable on admission
- Measure body weight
- Assess vital signs, chart temperature 4 hourly
- Observe for evidence of bleeding, especially melaena or bleeding per
- vagina and quantify the amount of bleeding.
- Maintain an intake and output chart
- Measure the urine output

- Urgent FBC on admission and review the report early. Then repeat
- FBC daily or more frequently if required.
- Inward PCV/HCT frequently as required.

Febrile Phase

- Ensure adequate fluid intake.
- Oral fluids are recommended if the child can consume an adequate amount.
- If the patient is vomiting, dehydrated, or unable to take sufficient oral fluids, consider intravenous (IV) fluids.
- The total fluid requirement (oral + IV) depends on the degree of dehydration.
- The infusion rate should be reduced once dehydration is corrected.
- When IV fluids are required during the febrile phase, use 5% dextrose in 0.9% NaCl. For infants below six months, use 5% dextrose in 0.45% NaCl.
- Administer paracetamol every six hours (15 mg/kg per dose), ensuring that the total dose does not exceed 60 mg/kg per 24 hours in children.
- Avoid all NSAIDs and steroids.

Identification of Critical Phase

Clinical status	Clinical deterioration with defervescence of fever.
Platelet count	below 100×10 9/L
HCT	progressively rising (>10%): Initiation of critical phase, 20% rising indicates significant plasma leakage, 30% rising indicates shock/impending shock.
Urine	Gradual reduction of urine output
Liver	New onset tender hepatomegaly
Pulse	Rising pulse rate disproportionate to the degree of fever
Capillary refill time	Prolonged
BP	Hypotension , pulse pressure >20 mmHg
Reduced HCT on the background of unstable vitals should suspicion of concealed bleeding	

Clinical Improvement Criteria

- Progressive waning of warning signs and general symptoms
- Stable vital signs (BP, Pulse rate, etc.)
- Increase amount of urine output
- Adequate oral intake
- Increases appetite.

Equilibrium phase: Readers are encouraged to refer to adult section for an in-depth understanding (page: 35)

Monitoring of febrile phase and critical phase (Use monitoring chart on annexure)

- Temperature
- Vital parameters - pulse, blood pressure (both systolic and diastolic), respiratory rate, capillary refill time and urine output 4 hourly (may need more frequent monitoring depending on the clinical situation)
- Intake and output
- FBC twice daily when platelet count is below 100000/mm3
- Inward PCV or HCT twice daily or more frequently when patient is in shock

Monitoring during convalescent phase.

- The frequency of vital sign monitoring can be reduced if the patient is stable. (Initially 3-4 hours later 6-12 hours.)
- High urine output is observed in most patient.
- Some patients may develop fluid overload during the convalescent phase. Therefore, it is important to observe for symptoms and signs of fluid overload.
- PCV monitoring can be reduced to daily and when platelet count is rising, PCV
- monitoring can be stopped in stable patients.
- Bradycardia is an expected finding in the convalescent period, which is usually
- asymptomatic and transient.

Note

- Identifying the beginning and the end of the critical phase is a key factor in guiding fluid therapy in DHF. It is important to monitor patients hourly in leaking phase. Monitor patients every 15 minutes interval in case of shock.
- If the patient presents in shock, the patient may have been in critical phase for a significant period of time, probably up to 24 hrs. Therefore, there is a possibility that some patients will have approximately another 24 hours remaining in the critical phase.
- If a patient is already dehydrated during the latter part of the febrile phase (due to vomiting, diarrhoea or lack of adequate fluid intake) and hydration is not corrected he or she might go into shock before 24 hours. In this instance the remaining duration of the critical phase may be more than 24 hours. However, until the very last stage of shock, a patient appears conscious and alert.

Fluid management:

Fluid replacement is the most important measure in the management of DF/DHF. Adequate fluid replacement is essential to avoid dehydration during the febrile phase, and to avoid shock. Careful fluid replacement during the equilibrium phase and convalescence/ reabsorption phase in a DHF patient is important to avoid fluid overload.

Febrile phase

- During febrile phase, fluid intake should be adequate to replace the urine output and insensible loss. Additional losses such as vomiting and diarrhoea should be replaced according to the volume loss. If the patient is dehydrated on admission, it should be corrected accordingly.
- For all In-ward patients, it is important to have an IV access by inserting preferably a small bore (24 G Yellow) cannula.

- Consider IV fluids for patients who are unable to take adequate volume of oral fluid, or patients with diarrhoea or vomiting.
- The recommended solutions for IV fluid therapy is 0.9% NS with 5% glucose (0.45% NS with 5% glucose for child below 6 months). The total amount of fluid (both IV and oral) should be limited to 50 ml/Kg/day
- However, if there is vomiting or diarrhoea this amount should be increased, and dehydration should be corrected according to IMCI protocol.
- Oral fluids should such as coconut water, other fruit juices, oral rehydration fluid and soup. Drinking plain water should be discouraged

Fluid management in critical Phase

It is important to replace fluid accurately during the critical phase. With plasma leakage, there is an additional loss of fluid from the intravascular compartment (in addition to urine and insensible loss).

- **Calculation of the fluid quota for the critical phase:**
  The amount of fluid recommended during the entire critical phase (irrespective of its length) should be: Maintenance fluid + 5% deficit (50ml/kg).

All patients will not need the full quota of M+ 5% fluid, and many may need less than this, as the rate, peak and duration of leaking are variable from patient to patient.

Calculations for normal maintenance of intravenous fluid infusion per hour: (Equivalent to Halliday-Segar formula)

For the 1st 10 kg - 100
ml/kg 2nd 10 kg - 50 ml/kg
From 20 kg and above 20 ml/kg

Example of fluid calculation for a child weight 25 kg

For the 1st 10 kg - 100 ml/kg = 1000 ml For the 2nd 10 kg - 50
ml/kg = 500 ml From 20 kg and above 20 ml/kg= 20*5 =100 ml .
Total maintenance = 1600ml
5% deficit is calculated as 50
ml/kg = 1250 ml Total = 1600 +
1250 ml = 2850

This is only a guide, and this volume is calculated considering a patient with fluid leakage amounting to moderate dehydration. Some patients might need a higher amount of fluid, especially if they develop shock

Note :

- Fluid input should be calculated using either the actual weight, the ideal weight for height or the adjusted body weight of the child in the following manner:
- If the actual weight is less than the ideal weight use the actual weight.
- If the actual weight is a little more than the ideal weight for the height, use the ideal weight.
- If there is a marked discrepancy between the ideal weight and the actual weight (≥2SD weight for height or BMI) then in such instances, it is best to use the adjusted body weight

See "Further reading "section for ideal body weight and adjusted body weight

Guide to the rate of fluid administration:

The fluid rate should be adjusted according to the rate of leaking**.**

Types of intravenous fluids

Choice of fluid for children

Crystalloid

In Febrile phase & non-shock critical stage:

As children are very prone to become hypoglycemic so fluid with glucose is the better choice for children. In Febrile phase & non-shock critical stage below 6 months 0.45% NS with 5% glucose and above 6 months 0.9% NS with 5% glucose should be used.

Compensated and decompensated shock:

In initial stage of shock 0.9% Normal saline or ringer's lactate should be used. But after initial critical stage when the child stable then choice of maintenance fluid should be same as non-shock critical phase.

Colloids:

Choice of colloids are as same as adult.
Dose of Starch (6%HES) and Dextran 40: 10ml/kg repeated dose
can be given (maximum 30ml/kg)

Colloids should be used: Readers are encouraged to refer to adult section for an in-depth understanding (page: 56)

Important discussion on fluid management

- When a child is managed at home, the recommended total fluid intake is 50 mL/kg over 24 hours.
- Hospitalized in Febrile Stage: If a child is hospitalized during the febrile stage, the total combined volume of intravenous and oral fluids should also be 50 mL/kg over 24 hours.
- Critical Phase (Shock/No Shock): The fluid volume requirements during the critical phase, both in shock and non-shock cases, will be discussed in detail later. The fluid volume in critical phase should be calculated based on the child's weight (... mL/kg).

NB: Following things should be considered during fluid management in dengue. After administration of crystalloid, hematocrit (Hct) typically decreases by 1–2 units. If the drop exceeds 3 units, hemorrhage should be suspected. A blood transfusion (10 mL/kg) or packed red blood cell transfusion (5 mL/kg) is expected to increase Hct by 3–5 points .

Non-shock Critical stage fluid management

The admitted children (DHF I&II) should be started with recommended fluid at a rate of 1.5ml/kg/hour and should be given for 6 hours. Choice of fluid could be 0.45% DNS for children below 6 months or 0.9% DNS for child above 6 months. If patient's vital signs are stable, then the escalation of fluid is not needed and the same rate can be maintained for a period of 48 hours. Remaining fluid as per weight can be taken orally. If the child un able to take proper amount of oral fluid, this amount can be given by intravenous route.

- After 6 hours of starting fluid, if patient have unstable vital signs and inadequate urine output management should be shifted to compensated/decompensated dengue shock treatment protocol.
- Patient should be monitored every 1 hour with special attention to vital signs, urine output, respiratory signs and haematocrit etc.
- Reassess the clinical status, repeat the haematocrit and review fluid infusion rates accordingly.
- Patients with warning signs should be monitored by health-care providers until the period of risk is over. A detailed fluid balance should be maintained.

Management of Dengue Shock Syndrome (Compensated & Decompensated) For clinical features readers are encouraged to refer to adult section for an in-depth understanding (page:34)

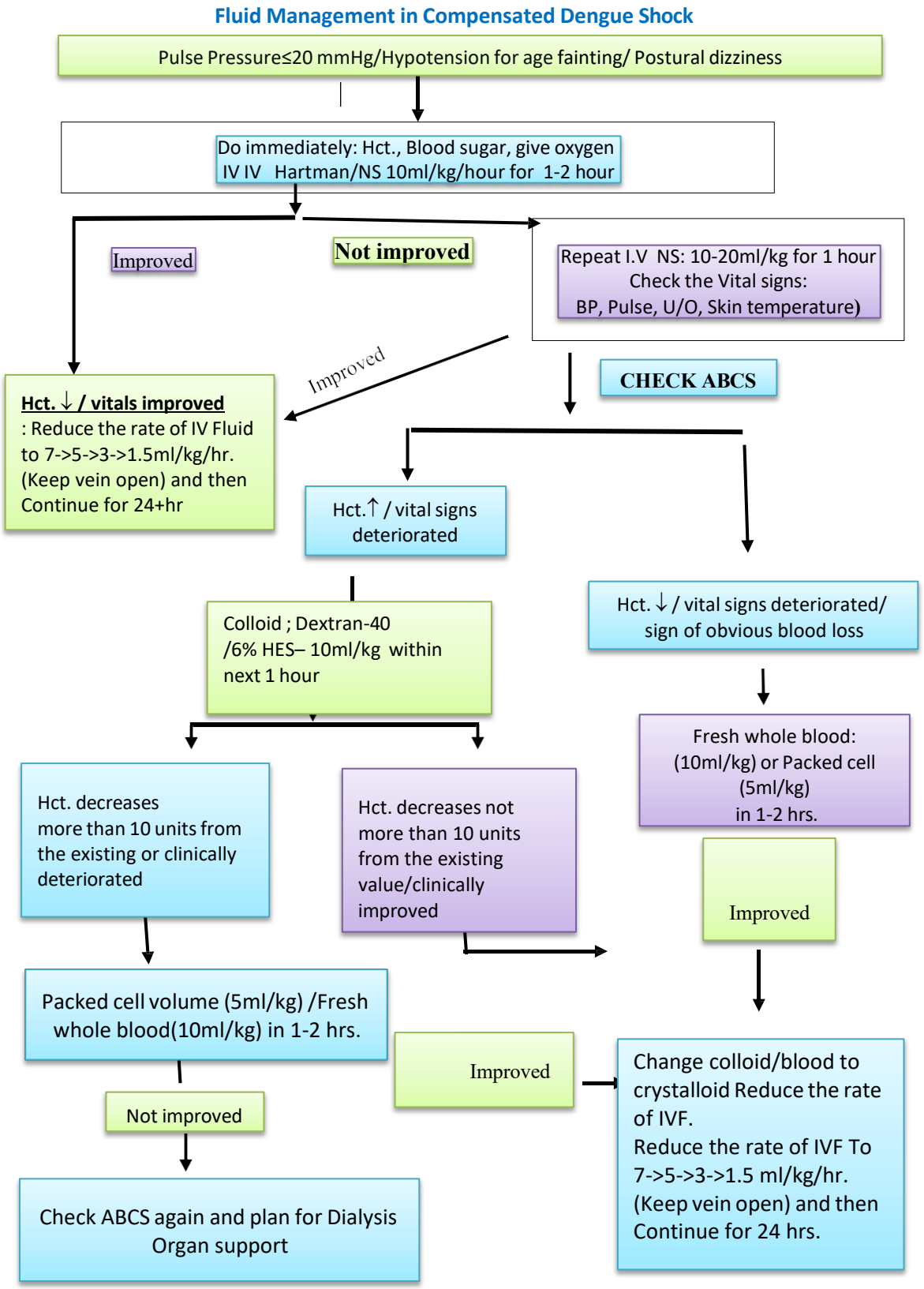


Figure 25: Flow diagram of fluid therapy for compensated shock in child

Management of Decompensated shock

Preferably this group of patients need to manage in ICU setting.

- **Oxygen should be started immediately**.
- The bolus 20 ml/kg crystalloids should be given within few minutes.
- If the vital signs and Hct improved, the fluid can be reduced
  a) From 10 ml/kg/hour for 1-2 hours, then
  b) from 7 ml/kg/ hour for 1-2 hours and then
  c) from 5 ml/kg/hour for 2-4 hours and then
  d) 3 ml/kg/ hour for another 2-4 hours. then
  e) 1.5 ml/kg/ hour

This rate (1.5 ml/kg/ hour) should be continued for at least 24 hours

- If there is no clinical improvement after bolus crystalloids, check Hct. Give another bolus of crystalloids.
- IF there is improvement (improvement in vital signs and Hct decreases, urine output 0.5 to 1.0 mL/kg/hour) then continue the crystalloids and reduce as stated before.
- If the Hct is rising, the fluid should be changed to a colloid. The preferred colloid is dextran or a starch-based fluid (if dextran is not available). The dose should be 10 ml/kg/ bolus, with a maximum dose of 30 ml/kg/24 hours.
- After giving the bolus crystalloids if the Hct is reduced but no improvement in vitals sign, then suspect concealed bleeding and blood transfusion should be started immediately (whole blood: 10ml/kg or packed RBC: 5ml/kg.)
- In refractory shock, correct ABCS (Acidosis, Bleeding, Calcium, Sugar) if deficiency present.
- In case of refractory shock, look for other causes of sepsis/ cardiogenic shock, significant intestinal bleeding, cytokine storm and treat accordingly
- If needed IV inotropes with crystalloids as per requirement should to be continued.
- In case of acidosis, hyperosmolar or ringers' lactate should not be used.
- During decompensated shock, Hct measurement should be measured in every hour ant it is more important than platelet count.

IV Fluid Therapy for Profound Shock (Decompensated Shock)

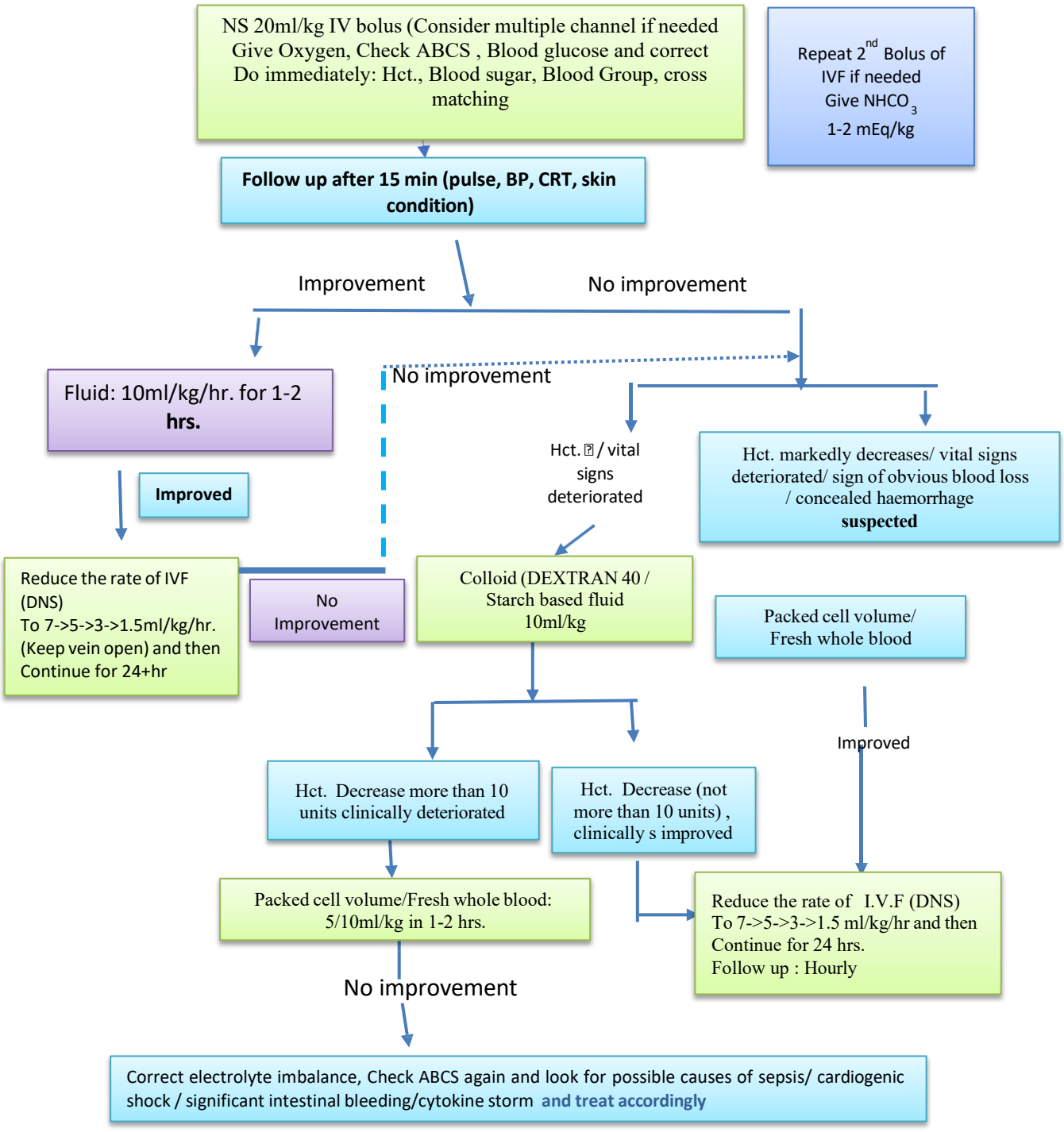


Figure 26: Flow diagram of fluid therapy for decompensated shock in child

Footnote: If history suggestive of previous multiple crystalloid shots, then the initial choice of fluid should be colloid. Continuing intravenous fluid therapy beyond the 48 hours of the critical phase will put the patient at risk of fluid over load and other complications such as thrombophlebitis

Patients not responding to fluid resuscitation (or with refractory shock)

If the patient is not responding to two boluses of crystalloid, contributory causes for shock other than plasma leakage should be considered.

These are,

- Acidosis -check venous blood gas including serum lactate
- Bleeding -check HCT
- Calcium- Check serum calcium and electrolytes (sodium and potassium)
- Sugar -check random capillary blood sugar

Other supportive measures

a) *Renal replacement therapy:* Renal failure is best managed with veno-venous hemodialysis. Children with shock, needing multiple vasoactive drugs, with acute kidney injury may need continuous renal replacement therapy (CRRT).

b) *Vasopressor and inotropic therapies*[51]*:* These are indicated if there is no improvement in blood pressure with adequate fluid replacement despite normal or raised CVP. Commonly used drugs include dopamine, epinephrine, and dobutamine. These drugs should be administered using a central line and the child should be managed preferably in an ICU.

Monitoring of a patient with evidence of compensated shock /decompensated shock.

- Vital parameters and CRFT should be checked every 15 minutes until the patient are haemodynamically stable.
- During intense fluid resuscitation, in ward HCT should be checked immediately before and 10-15 minutes after each fluid bolus and at least two to three hourly.
- If the shock is prolonged (not responding to initial fluid bolus) an indwelling urinary catheter should be inserted and urine output should be measured hourly. UOP of 0.5 ml to 1 ml/kg body weight / hour is adequate during this period. Overenthusiastic fluid replacement to achieve a higher UOP may lead to fluid overload.
- Liver profile, blood sugar, serum calcium, serum electrolytes, serum creatinine, clotting profile and venous blood gases and Lactate levels should be done in complicated cases such as prolonged shock, not responding to adequate fluid resuscitation, liver involvement and renal involvement.
- Once the patient is stabilized monitoring can be spaced out. Monitoring of vital parameters 2-4 hourly and UOP every 4 hourly would be adequate depending on the patients haemodynamic status.

When to stop intravenous fluid therapy

- Stable BP, pulse, peripheral perfusion (CRT <2sec)
- Improvement of urine output (>1ml/kg/hour)
- Cessation of plasma leakage and bleeding
- Haematocrit decreases in the presence of a good pulse volume
- Absence of fever (without the use of antipyretics) for more than 24–48 hours
- Resolving abdominal symptom

Fluid Overloaded Patient

Clinical features of fluid overload:

- Rapid breathing / respiratory distress (if respiratory rate increases 5 breaths/minute from previous follow up in indicates fluid over load in children).
- Increase heart rate (if heart rate increases by 25 beat /minute from previous follow up in indicates fluid over load in children)
- Suprasternal in-drawing and intercostal recession (in children)
- Basal crepitations
- Increased jugular venous pressure (JVP)
- Puffy face & leg oedema.

Management of fluid overload:

- Review the total intravenous fluid therapy, clinical course. Check for ABCS.
- Stop all IV fluid if patient is not in shock
- In the early stage of fluid overload, switch from crystalloid to colloid solutions as bolus fluids. Dextran 40 is effective as 10 ml/kg bolus infusions, but the dose is restricted to 30 ml/kg/day because of its renal effects.
- In the late stage of fluid overload or those with frank pulmonary oedema, furosemide may be administered if the patient has stable vital signs.
- If they are in shock, together with fluid overload 10 ml/kg/h of colloid (dextran) should be given. When the blood pressure is stable, usually within 10 to 30 minutes of infusion, administer IV furosemide and continue with dextran infusion until completion.
- These patients should have a urinary catheter to monitor hourly urine output.
- After administration of furosemide, the vital signs should be monitored every 15 minutes for one hour to note its effects.
- If there is no urine output in response to furosemide, check the intravascular volume status (CVP or lactate).

DHF patients are very sensitive to furosemide. So the dose should be smaller than the usual dose (0.1 mg/kg as a bolus). This can be repeated if necessary

Flow Diagram for the Management of Fluid Overload

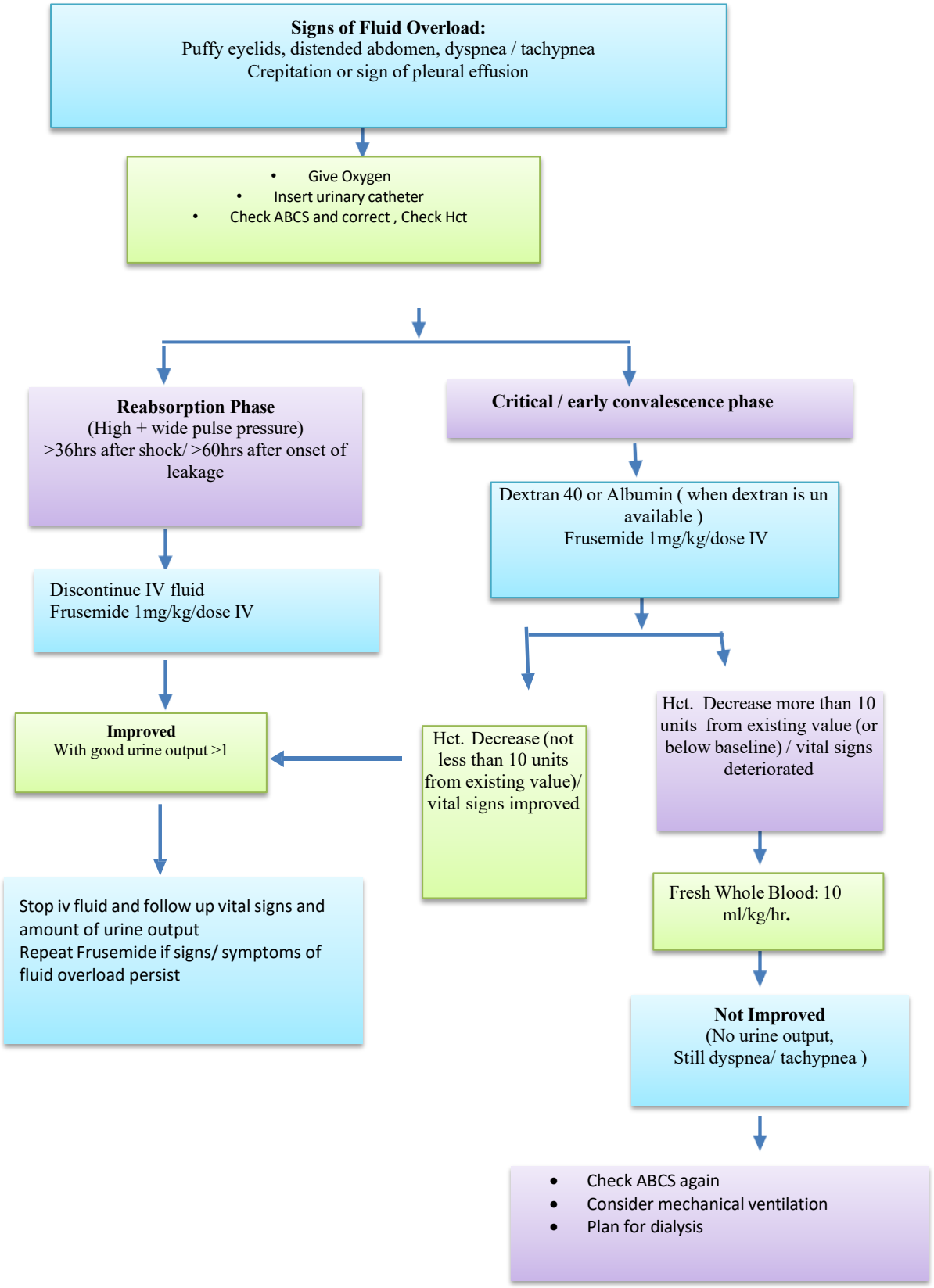


Figure 27: Flow diagram for the management of fluid overload in child

The following points should be noted:

- These patients should have a urinary catheter to monitor hourly urine output
- Intravenous Furosemide should be administered during dextran infusion because the hyper tonic nature of dextran will maintain the intra vascular volume while furosemide depletes in the intravascular compartment. After administration of furosemide, the vital signs should be monitored every 15 to 30 minutes interval for one hour to note its effects.
- In cases with no response to furosemide (no urine obtained), repeated doses of furosemide and doubling of the dose are recommended. If oliguric renal failure is established, renal replacement therapy is to be done as soon as possible. These cases have poor prognosis.
- If there is no urine output in response to furosemide, check the intravascular volume status (CVP or lactate). If this is adequate, pre-renal failure is excluded, implying that the patient is in an acute kidney injury state. These patients may require ICU/dialysis support soon. If the intravascular volume is inadequate or the blood pressure is unstable, check the ABCS and other electrolyte imbalances
- Pleural and/or abdominal tapping may be indicated and can be life-saving in cases with severe respiratory distress and failure of the above management. This has to be done with extreme caution because traumatic bleeding is the most serious complication and can be detrimental. Discussions and explanations about the complications and the prognosis with families are mandatory before performing this procedure.

  Treatment of Bleeding: Readers are encouraged to refer to adult section for an in-depth understanding (page:61)

  Note:
  - Even with bleeding, the Hct drop may take time (4-5 hours). When the patient does not show improvement, it is important to repeat Hct frequently.
  - Haemoglobin level may remain normal despite significant blood loss.

If there is coagulopathy due to hepatic involvement, fresh frozen plasma can be given.

Calcium Replacement: Readers are encouraged to refer to adult section for an in-depth understanding (page:62)

Glucose control

- In infants and children, blood glucose should be monitored frequently during the critical phase and into the recovery phase if the oral intake is still reduced.
- However, if hyperglycemia is persistent, undiagnosed diabetes mellitus or Impaired glucose tolerance should be considered and intravenous insulin therapy initiated.
- Hypoglycemia should be treated accordingly. If the capillary blood sugar is less than 70 mg/dL administer 10% dextrose, 2 ml/kg followed by 0.9% NaCl with 5% dextrose infusion.
- Electrolyte imbalance should be corrected according to standard guideline
- Antibiotic can be given if there is co infection.

Metabolic acidosis: Readers are encouraged to refer to adult section for an in-depth understanding (page:63)

Encephalopathy: Readers are encouraged to refer to adult section for an in-depth understanding (page:64)

Haemophagocytic lymphohistiocytosis (HLH): Readers are encouraged to refer to adult section for an in-depth understanding (page:66)

Management of Diarrhoea in Dengue Patients

- Dengue patients may have diarrhea and require proper management.
- Fluid management should be done according to the IMCI protocol.
- Since fluid overload is very common in children, I.V. fluids should be administered cautiously and oral saline (ORS) should be encouraged.
- If there is no dehydration and the child is below 5 years of age, the amount of ORS should be given as **1 teaspoon per kilogram of body weight after every episode of purging**.
- **For some dehydration (Plan B):** If the patient cannot tolerate oral fluids, administer cholera saline I.V. in the same amount as recommended for some dehydration (75 ml/kg) over 4 hours. Frequent follow-ups should be conducted. If signs of dehydration resolve during follow- up, discontinue the cholera saline immediately.
- **For severe dehydration (Plan C):** Manage according to Plan C of the IMCI protocol. Administer cholera saline I.V. at 100 ml/kg. The duration of administration should be based on age: within 6 hours for children below one year and within 3 hours for children above one year. Frequent follow-ups are essential. If signs of dehydration resolve during follow-up, discontinue the cholera saline immediately.
- Monitoring urine output is essential and must be observed closely.

Discharge Criteria:

- Stable pulse, blood pressure and breathing rate.
- Normal temperature.
- No evidence of external or internal bleeding.
- Return of appetite.
- No vomiting, no abdominal pain.
- Good urinary output.
- Stable haematocrit at baseline level.
- Convalescent confluent petechiae rash or itching, especially on the extremities.
- No fever for at least 24 hours without the usage of antipyretic drugs
- At least two days have lapsed after recovery from shock
- Good general condition with improving appetite
- Normal HCT at baseline value or around 38 - 40 % when baseline value is not known
- No distress from pleural effusions
- No ascites
- Platelet count has risen above 50,000 /mm3
- No other complications

Further reading

Recommended Size of BP cuffs:

- Using a wrong sized blood pressure cuff can affect accuracy up to 30 mmHg.
- The American Heart Association recommends –
- Cuff bladder width should be 40% of the arm circumference
- Cuff bladder length should be 80% of the arm circumference

Size of BP cuff by age

- Newborns and premature infants 4 × 8 cm
- Infants 6 × 12 cm
- Older children 9 × 18 cm

Blood pressure by age

Age	Systolic pressure	Diastolic pressure	Systolic hypotension
Birth(12 h, <1000gm)	39-59	16-36	<40-50
Birth(12 h, 3 kg)	60-76	21-45	<50
Neonate (96 hrs.)	67-84	35-53	<60
Infant (1-12 months)	72-104	37-56	<70
Toddler (1-2 yrs.)	86-106	42-63	<70+ (age in year × 2)
Preschool (3-5 yrs.)	89-112	46-72	<70 + (age in year × 2)
School – age (6-11 yrs.)	97-115	57-76	<70 + (age in year × 2)
Preadolescent (10-11yrs.)	102-120	61-80	<90
Adolescent (12-15 yrs.)	110-131	64-83	<90

(Ref: National Dengue Guideline 2018, Annex 4)

Doses for Paediatrics patients:

- Paracetamol: 15mg.kg/dose
- Dextran: 10 ml/kg bolus (maximum: 30 ml/kg/24 hours)
- 6% HES: 10 ml/kg bolus (maximum: 30 ml/kg/24 hours)
- Human albumin 20%: 0.5-1gm/kg, over 2-4 hours IV (5mk/kg)
- Whole blood: 10ml/kg
- Packed RBC: 5ml/kg.)
- $NHCO_3$: 1-2 mEq/kg
- Dopamine: 10-15 mcg/kg/min

Ideal Body Weight Tables

Age (yr)	Boys (kg)	Girls (kg)
2	13	12
3	14	14
4	16	16
5	18	18
6	21	20
7	23	23
8	26	26
9	29	29
10	32	33
11	36	37
12	40	42
13	45	46
14	51	49
15	56	52
16	61	54
17	65	55
18	67	56
19	69	57

Height	Males (kg)	Females (kg)
5' (152 cm)	50	45
5'1" (155 cm)	52	48
5'2" (157 cm)	54	50
5'3" (160 cm)	57	52
5'4" (163 cm)	59	55
5'5" (165 cm)	61	57
5'6" (168 cm)	64	59
5'7" (170 cm)	66	62
5'8" (173 cm)	68	64
5'9" (175 cm)	71	66
5'10" (178 cm)	73	69
5'11" (180 cm)	76	71
6' (183 cm)	78	73
6'1" (185 cm)	80	75

1 kg = 2.2 pounds

Calculation of adjusted body weight (Source : Guidelines on Management of Dengue Fever & Dengue Haemorrhagic Fever in Children and Adolescents. *Colombo: Ministry of Health Sri Lanka; [2023]. p.46.*

Calculation of the adjusted body weight

$$\text{Adjusted body weight} = 0.4\left(\text{Actual body weight} - \text{Ideal body weight}\right) + \text{Ideal body weight}$$

Dengue fever and Pregnancy

Chapter-7

7.1 Introduction:

Dengue fever (DF) in pregnancy is important because it is preventable and treatable, but may sometimes complicated enough to cause maternal & fetal death. All pregnant women with fever irrespective of trimester should be given due importance for various reasons including - maternal and fetal well-being, development of disease related life-threatening complications and the management challenges due to physiological changes in pregnancy.

Concern regarding women who are pregnant getting infected with dengue virus has been heightened in recent years. 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 practicing clinicians based on best available evidence at the time of writing. Further, there has been a substantial reduction in complications and unwanted deaths in clinical settings practicing the guidance given here in.

Key points

- Diagnose DF as per national guideline
- Provide due importance to the impact of DF in pregnancy, every febrile illness in pregnancy should be consider as dengue as part of early differential diagnosis.
- Differentiate DF from other differentials
- Explain effect of dengue on pregnancy and effect of pregnancy on dengue
- Physiological changes in pregnancy that may make the diagnosis and assessment of plasma leakage challenging
- Confusion or misdiagnosis and challenges with other complications of pregnancy at different gestation
- Assess gestational age and phase of dengue
- Perform proper triage for dengue patients
- Manage a case of dengue in pregnancy with or without complications in different situations
- Organize multidisciplinary team approach for management of dengue in pregnancy
- Sonographic assessment of fluid leakage
- Regular haematocrit monitoring
- Ensure maternal and fetal wellbeing monitoring
- Manage with multidisciplinary (MDT) approaches in inevitable delivery during critical phase
- Impact of dengue at intrapartum and postpartum period and it's management
- Inform and update patient's family member regularly and before any intervention

Factors to be consider in DF in pregnancy:

- The gestation and the phase of dengue are important factors in determining the management and should manage as per guideline.
- Effects of Pregnancy on dengue
- Impact on physiology of pregnancy.

7.2 Impact of pregnancy on DF:

The following physiological changes in pregnancy may make the diagnosis and assessment of plasma leakage challenging:

- Elevation of Hct in dengue is masked by hemodilution due to increase in plasma volume especially in the 2nd and 3rd trimester.
- Serial Hct measurement is crucial for disease monitoring in pregnancy.
- The detection of third space fluid accumulation is difficult due to the presence of gravid uterus.
- Baseline blood pressure is often lower and pulse pressure wider.
- Baseline heart rate may be higher.
- HCO3 level lower

Impact of DF on pregnancy and delivery

- Early abortion (3%-13%).
- Embryopathy especially neural tube defect.
- Antepartum haemorrhage (APH) due to retro placental haemorrhage or abruptio placenta
- Preterm birth (3%-33%).
- Low-birth weight (9%-16%).
- IUGR.
- Fetal distress,
- IUD or still birth (4.7%-13 %.)
- Increased incidence of caesarean deliveries.
- Post Partum Haemorrhage (PPH).

Confusion or Misdiagnosis and Challenges with other complications of pregnancy:

- Sever preeclampsia (PE)
- HELLP syndrome (Hemolysis, Elevated Liver Enzymes, Low Platelet)
- Abruptio Placenta or concealed haemorrhage.

Significant impact of DF at parturition

- Severe bleeding may complicate delivery and/or surgical procedures performed on pregnant patients with dengue during the critical phase.

Risk of vertical transmission:

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

- Disruption of placental barrier
- Prolong viremia
- Reported 1.6% to 10.5

Causes of Maternal death

- Sever Antepartum haemorrhage (APH)
- Sever Post-partum haemorrhage (PPH)
- Dengue shock syndrome (DSS)
- Multi organ failure (MOF)

Causes of Fetal death

- Fetal distress
- Fetal circulatory insufficiency
- Fetal coagulopathy

7.3 Early management and admission/referral:

- All pregnant women with acute fever should be comprehensively assessed and monitored closely and also suspect as dengue.
- Admission note / referral letter should include the necessary details and vital parameters.

7.4 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 CBC.
- 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 CBC 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 1st and 2nd trimester if the patient is haemodynamically stable, admit to ward. If-haemodynamically unstable admit to HDU.
- In 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

7.5 Level of care of DF with Pregnancy by whom and where?

Level of care:

Primary (OPD/Clinic/UHFWC)	Clinical assessment- Stable patient: Diagnosis & treatment Warning sign: Ref to tertiary level
Secondary (UHTC, smaller hospitals without ICU/HDU/NICU)	Clinical assessment- Stable patient: Treatment Warning sign: Ref to tertiary level
Tertiary care center	All complicated DF & DHF

Table 16: Level of care of DF with pregnancy.

7.6 Admission criteria:

- All pregnant women with acute onset of fever should be advised to get admitted early to a hospital, where specialists cover is available (despite normal CBC) for further care.
- First contact doctor should make a comprehensive assessment of the patient in order to decide on resuscitation at management at Obstetric/Medical Unit, irrespective of the duration of fever.
- Admission referral letter should include the necessary details and vital parameters

7.7 Inpatient management of dengue in pregnancy:

- Management of dengue in pregnancy should be of multi-disciplinary approach involving Obstetric team, Internist, Neonatologist, Anesthesiologist and Nurses/Midwives
- 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).

Management according to trimester by whom and where?

- All pregnant patients with fever irrespective of the trimester, should be first admitted to the medicine ward (without any obstetric complication) where obstetric unit will be called in where initial assessment and management plans are to be decided.
- Further management should be done in consultation with the medical multidisciplinary team (MDT).
- Suggested place of management is as follows, to be decided with the consensus of Medical and obstetric team will be immediately mobilized and if patient's condition permits. If any obstetric complication develops or obstetric intervention is needed. A obstetrician should be called or patient is referred/sent to obstetric ward similarly if any obstetric complication arises when a pregnant patient with dengue, admitted in medicine ward of HDU.

Clinical Status`		1st Trimester	2nd Trimester	3rd Trimester (not in labour)
DF with obstetric complication/ emergency	Whom	Obstetric and Medical team	Obstetric and Medical team	Obstetric and Medical team
	Where	Obstetric Ward	Obstetric Ward	Obstetric Ward
DF/DHF in uncomplicated pregnancy	Whom	Obstetric and Medical team	Obstetric and Medical team	Obstetric and Medical team
	Where	Medical Ward HDU	Medical Ward HDU	Medical Ward HDU
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

Table 17: Showing obstetric case management place and person.

7.8 Assessment of patient once admitted to relevant unit:

A. Medical assessment should include:

- Febrile phase monitoring (patient not leaking yet)
- Critical phase monitoring in a patient with plasma leakage

B. Obstetric (Maternal & Fetal) assessment:

- Should be done daily or more often depending on the trimester.

C. Investigations;

- Serial CBC & Hct count
- Imaging 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.

7.8.1 Afebrile 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.
- Requires close monitoring until full recovery by trained nurse.
- 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 CBC and other investigations as necessary (e.g. LFT).
- Notify on-call doctor immediately if any high-risk features are noticed (warning signs, derangement of vital signs reduced UOP and rising haematocrit.

7.8.2 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 woman with dengue illness when the platelet counts drops ≤130x109/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 cannula.

Monitoring Parameters	Frequency
General Well-being: • Appetite, vomiting, bleeding, giddiness, intense thirst, restlessness, clouding of consciousness	• At least twice-daily
Vital signs: • Temperature, PR, BP, PP and RR) by multi-para monitor) • Pulse volume and CRFT **Haematocrit (HCT/PV):** • In uncomplicated DHF • In unstable patients or those with suspected/ massive bleeding • Administration of fluid bolus (NS/ Dextran-40/ blood)	• In non-shock patients hourly • In shock patients every 15 minutes (until BP restored) • Every 3 hours • More frequently if necessary • Before and after each fluid bolus
Urine Output: • Maintained urine output 0.5-1.0ml/kg/h (calculated for pre-pregnancy body weight). Preferred UOP in pregnancy is 0.75ml/kg/h	• Measure 3-4 hourly and calculate for every hour
Platelet count	• Measure 6-24 hourly

Table 18: Critical phase monitoring during pregnancy

7.8.3 Features of dengue shock in pregnancy:

Compensated shock: Readers are encouraged to refer to adult section for an in-depth understanding (page:34)

Decompensated shock: Readers are encouraged to refer to adult section for an in-depth understanding (page: 34)
In pregnant women with decompensated shock, early assessment of degree of shock is important. Such patients can be further classified as:

Prolonged shock and profound shock–

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

7.8.4 Special Clinical Situations with Pregnancy

Dengue syndromes with pregnancy with the co-morbid diseases/ situations demand special attention. Even in the well-equipped specialized center the risk of mortality will be very high.

Some common situations are as follows:

- Pregnancy with severe anaemia
- Preeclampsia and HELLP Syndrome
- Diabetes
- Chronic Liver Disease
- Chronic Kidney Disease
- Cardiac diseases: Heart Failure, Ischemic Heart Disease, HTN
- Autoimmune disorder like SLE
- Immunocompromised Patient
- Patient with Co-Existing Infection

These Patient needs special attention and should be manage at Tertiary Level Hospital and by Multi-disciplinary team approaches

B. Obstetrical Management:

Monitoring of Dengue patient with pregnancy- In addition to close monitoring of the pregnant patient with dengue on medical parameters. Obstetric care and fetal monitoring has to be continued.

Fetal well-being evaluation

Methods of fetal well-being evaluation

- Gestational age
- Fetal movement (daily)
- Fetal Heart Rate (FHR- 06 hourly)
- Cardiotocography (CTG- daily)
    - Baseline fetal heart rate (110-180 b/min)
    - Beat to beat variability (5-25 b/min)
    - Acceleration (2 or more)
    - Deceleration (No deceleration)
- USG of pregnancy profile (as needed)
    - Fetal Heart rate
    - Fetal weight
    - Fetal Presentation
    - AFI
    - Placental position and maturation

Biophysical profile (BPP): weekly / twice weekly

Biophysical profile:

Sl. no	Parameters	Minimal normal criteria	Score
1	Non stress test (NST)	Reactive pattern	2
2	Fetal breathing movement	1 episode lasting>30 sec	2
3	Gross body movement	3 discrete body/ limb movements	2
4	Fetal muscle tone	1 episode of extension (limb or trunk)with return of flexion	2
5	Amniotic fluid	1 pocket measuring 2cm in twoperpendicular planes	2

Table 19: Biophysical profile

BPP Scoring interpretation and management:

BPP Score	Interpretation	Management
8-10	No fetal asphyxia	Repeat testing at weekly intervalor more
6	Suspect chronic asphyxia	If > 36 weeks deliver; but If L/S < 2.0 repeat test in 4-6 hours
4	Suspect chronic asphyxia	If >/ 36 weeks deliver, if < 32 weeks repeat testing in 4-6 hours
0-2	Strongly suspect asphyxia	Test for 120 minutes → persistentscore < 4 → deliver regardless of gestational age

Table 20: BPP Scoring interpretation and management

Note - When the patient in critical phase then we will try to delay the delivery to prevent complications.

Time and frequency of investigations:

- Test should be done during first consultation to get the baseline information.
- Follow up testing cone depending on the conditions of the patients.
- CBC and Hct should be done daily once DHF is suspected.
- A regular Hct is more important for management than the platelet count.
- Elevation of Hct in dengue is masked by haemodilution due to increase in plasma volume especially in the 2nd and 3rd trimester
- Even in sever dengue with shock hourly haematocrit is crucial for management.
- For fetal wellbeing after 32 weeks of pregnancy CTG daily & BPP weekly

Recommendations for diagnosis:

- The baseline Hct and WBC should be established as early as possible in all patients with suspected dengue.
- Serial CBC and Hct must be monitored as the disease progress.
- Once the platelet count begins to rise and reaches 50,000/mm, 3 daily lab evaluation may be discontinued.

Complication:

- Premature fetal loss or vertical transmission in Dengue infection may be one of the grave fetal complications in pregnancy.
- The vertical transmission in fetus is evidenced by fever, thrombocytopenia, raised liver enzymes, gastric bleeding, pleural effusion, convalescent rash and Dengue- specific IgM (+).
- The important maternal complications include thrombocytopenia, raised liver enzymes, febrile illness, gum bleeding and bilateral pleural effusions.

Management:

- Uncomplicated pregnancy may become complicated with DHF/DSS at any time.
- Delivery preferably should be conducted in a tertiary hospital where all advanced facilities are available.
- The normal physiological changes in pregnancy make the diagnosis and assessment of plasma leakage difficult. Therefore, the following baseline parameters should be noted as early as possible on the first day of illness:
- Pulse, blood pressure (BP), pulse pressure. (Baseline BP is often lower and pulse pressure wider & heart rate may be higher)
- CBC - (Haemoglobin, Hct & platelet count may be lower than in nonpregnant patient)
- SGOT/SGPT
- Clinical detection of pleural effusion and ascites may be difficult due to the presence of gravid uterus. Use of Ultra Sound Scan to detect the following, is advisable
- Pleural effusion
- Ascites (Gallbladder wall oedema may be seen in both DF & DHF)

Fluid management:

Generally, the presentation and clinical course of dengue in pregnant women is similar to that in non-pregnant individuals.
The fluid volume for the critical period (M+5%) for apregnant mother should be calculated (based on the weight prior to pregnancy/ early pregnancy body weight)

Early pregnancy Management Precautions:

Dengue Virus Infection in early pregnancy should be managed very carefully. It is important to keep in mind for the obstetricians that don't take any steps or intervention which will be life threatening for the mother and also for fetus.

Avoid/ No (In early pregnancy):

- Medical termination of pregnancy
- Amniocentesis
- Chorionic villous sampling
- Cordocentesis
- MR
- D & C

Management of pregnant patients with DF/DHF close to delivery:

Risk of bleeding is at its highest during the period of plasma leakage (critical phase). Therefore, unless to save mothers life, avoid lower uterine segment caesarean Section (LUCS) or induction of labour during the critical (plasma leakage) phase. Obstetric procedures (such as amniocentesis or external cephalic version) should be avoided during the illness. If obstetric procedures are to be undertaken,

- Maintain the platelet count above 50,000/mm3 Single donor platelet transfusion is preferred (if available).
- If patient goes into spontaneous labour during critical phase take steps to prevent vaginal tears by performing an episiotomy.
- In a case of fetal compromise priority should be given to the mother's life and decision making should involve the multidisciplinary team.
- Counseling the family on the probable outcome is essential.

Labour and Delivery management:

It is the most crucial point of pregnant woman with dengue virus infection that they should be managed properly during the labour and delivery time. It includes

- Delivery precaution
- Hospital delivery
- Blood available
- Multidisciplinary approaches
- Team of skilled Obstetrician, Physicians, Anestheticts, Neonatologist, ICU Specialist
- No Planed Induction of labour or elective cesarean section
- Unless to save mothers life, avoid LUCS or induction of labour during the Critical phase.
- Obstetric procedures external cephalic version or internal podalic version should be avoided during the critical phase.
- No episiotomy.
- No instrumental delivery.

If Premature labour:

- Advise to delay delivery till acute infection resolves.
- Tocolytics may be given.
- Inj. steroid I/V given for the Lung maturation of fetus.
- Close fetal monitoring.

Inevitable delivery during critical phase:

- If delivery is inevitable, bleeding should be anticipated and closely monitored.
- Blood and blood products should be cross-matched and saved in preparation for delivery.
- Trauma or injury should be kept to the minimum if possible.
- Avoid instrumental delivery or episiotomy.
- It is essential to check for complete removal of the palccenta after delivery.
- Fresh whole blood/fresh packed red cells transfusion should be administred as soon as possible if significant bleeding occurs. If blood loss can be quantified it should be replaced immediately.
- Do not wait for blood loss to exceed 500ml blood before replacement, as in postpartum haemorrhage.
    - Do not wait for the haematocrit to decrease to low levels.
- Prophylactic platelet transfusion is NOT recommended unless delivery is inevitable (in coming 6 hours) platelet count > 50000/CC, and 75000/cc for operative delivery.
    - If operative delivery is mandatory in a patient with DHF, proper assessment of the patient, hematological and biochemical investigations should be available immediately prior to surgery.
    - Fresh blood and or platelet concentrate also has to be made available prior to surgery.
    - Fluid replacement should be according to stage the of DHF. Other treatment is to be given as usual tailored to the need.
- Single donor platelet transfusion is preferred, if platelet transfusion is necessary.
- Oxytocin infusion should be commenced to contract the uterus after delivery to prevent postpartum haemorrhage.
- Active Management of Third stage of labour (AMTSL).
- Misoprostol may be given for PPH Prophylaxis/treatment.
- Prophylactic Inj. Tranexamic acid 1 gm in 10ml administrated slowly with a second dose 1 gm IV if bleeding continues after 30 min.
- Prophylactic balloon tamponade given if delivery occur in critical phase of dengue.
- Intramuscular injections or skin prick for blood sugar monitoring should be avoided.
    - In a case of fetal compromise priority should be given to the mother's life and decision making should involve the multidisciplinary team.
    - Counseling the family on the probable outcome is essential.

Management of patients with DF/DHF during immediate postpartum:

Dengue fever should be suspected in patients having fever in the immediate post-partum period since this may be overlooked. Early referral to a physician is recommended.

For newborn:

- Early cord clamping advised.

Cord blood will send for:

- CBC
- NS1 anti gent test
- Dengue antibody test
- Blood grouping and Rh typing

Post-delivery:

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

Breast Feeding:

- Breast feeding encouraged and allowed.

Signs of recovery:

- Stable pulse
- Blood presure and breatheing rate
- Normal temperature
- No evidence of external or internal bleeding
- Return of appetite
- No vomiting, no abdominal pain
- Good urinary output
- Stable haematocrit at baseline level
- Convalescent confluent petechial rash or itching, especially on the extremities

Discharge criteria:

- Must be afebrile for 48 hours (without antipyretics)
- Stable haematocrit for at least 24 hours (baseline value or around 38-40% when baseline value is not known)
- Rising trend in platelet count (above 50000/mm^3)
- No dyspnea or respiratory distress attributable to pleural effusion or ascites
- No ascites
- No or minimal visible bleeding
- Fully recovered organ dysfunction
- No excessive P/V bleeding (APH or PPH)
- Stable maternal & fetal condition

Management of women with DF/DHF and gynaecological condition/complication:

1. Elective intervention/surgery has to be delayed till she is cured
2. In case of emergency try to take conservative measure.
3. If surgical interventions has to be undertaken it has to be a tertiary hospital/with facility for blood transfusion and HPD/ICU support.
4. Female patient with DF/DHF may present with irregular vaginal bleeding or menorrhagia tranexamic acid and progesterone may be the performed medication.

Special Clinical Situations

Chapter-8

8.1 Special Clinical Situations:

DF and DHF may develop in a patient stop some other clinical situations. Dengue syndromes with the co-morbid diseases/ situations demand special attention. Even in the we equipped specialized center the risk of mortality will be very high.

Some common situations are as follows:

- Elderly patient
- Mandatory Surgery
- Dengue fever and antiplatelet/anticoagulant drugs.
- Chronic Liver Disease
- Chronic Kidney Disease
- Cardiac diseases: Heart Failure, Ischemic Heart Disease, HTN
- Diabetes and Dengue
- Patient on steroid therapy
- Fluid hypersensitivity and anaphylaxis
- Cancer patient
- Immunocompromised Patient
- Patient with Co-Existing Infection

Dengue in the elderly:

Clinical manifestations

- Little is known about dengue in the elderly.
- Clinical manifestations of dengue in the elderly are similar to those of younger adults.
- However, rash, hepatomegaly and mucocutaneous haemorrhage are less frequent but gastrointestinal tract bleeding and microhaematuria are more common.
- The elderly has significantly lower incidences of fever, abdominal pain, bone pain and rashes.
- Higher frequencies of concurrent bacteraemia, gastrointestinal bleeding, acute renal failure, and pleural effusion.
- Higher incidence of prolonged prothrombin time and lower mean haemoglobin levels than younger adult patients.
- A higher incidence of plasma leakage and case fatalities has been reported in the elderly compared to young adult dengue patients.

Issues in management:

- About 10% of elderly dengue patients may have no complaints of fever
- Higher rate of acute renal failure
- The impact of increased co-morbidities.
- Ageing-related decline in cardiopulmonary function is another important consideration during fluid replacement and/or resuscitation in dengue illness.
- Complications such as congestive heart failure and acute pulmonary oedema may occur.
- Frequent assessments and adjustments of the fluid regime are required to avoid or to minimize such complications.

Mandatory Surgery:

- If surgery is mandatory in a patient with DHF, proper assessment of the patient, hematological and biochemical investigations should be available immediately prior to surgery.
- Fresh blood and or platelet concentrate also has to be made available prior to surgery.
- Platelet count should be raised up to 100000/mm3.
- Fluid replacement should be according to stage the of DHF. Other treatment is to be given as usual tailored to the need.

Dengue fever and antiplatelet/anticoagulant drugs:

- There are limited available evidence and no guideline on how to manage anticoagulant in dengue patients with prosthetic valves or venous thromboembolism (VTE), and antiplatelet in dengue patients with cardiovascular disease that required mono or dual antiplatelet therapy (DAPT).
- The risks of bleeding need to be balanced against the risks of thrombosis from temporary withhold anticoagulant or antiplatelet. Hence, the case management is case to case basis, based on expert opinion from various managing team with extrapolated evidence from non- dengue patients.
- However, thrombocytopenia, platelet dysfunction and coagulopathies in dengue fever are dynamics.

Dengue fever without significant bleeding:

Withhold anticoagulant /antiplatelet in DF with any of following:

a) Severe Dengue
b) Platelet < 50 x 109/L

- Consider withhold anticoagulant / antiplatelet in DF in febrile phase with warning signs or platelet reducing trend to between 50 -100 x 109/L, especially in those with high risk of bleeding, but relatively lower thrombosis risk.
- If anticoagulant needed for dengue patients with high risk of thrombosis but relatively low risk of bleeding, switch DOAC/ Warfarin (VKA) to LMWH/ Conventional heparin infusion when INR subtherapeutic if platelet 50 -100 x 109/L or even earlier with platelet > 100 x 109/L in febrile phase.
- Multi-disciplinary team management with cardiologist, haematologist, intensivist/ anesthetist, patient and patient's family for decision making.

Chronic Liver Disease (CLD):

- The disease may be decompensated in DHF who was well compensated before Dengue episode.
- As DHF involves in hepatic enzyme elevation so critical patient care and regular LFT should be done.
- Decompensated CLD should be managed as non-infected patient.
- Platelet concentrate & fresh blood maybe required. Patient should be treated in a hospital where facilities are available.

Chronic Kidney Disease (CKD):

- Dengue patients with Chronic Kidney Disease (CKD) have a significantly higher risk of severe dengue and mortality. The outcome correlates with the renal function.
- The warning signs of severe dengue are similar to those of uraemia in CKD.
- Ascites and/or pleural effusion, and signs of plasma leakage in dengue, are not uncommon findings in patients with CKD and fluid retention.
- The ambiguity of these symptoms and signs could delay the recognition of plasma leakage and severe dengue.
- Patients with CKD have a low baseline haematocrit and platelet count
- A low baseline platelet count is not an uncommon finding in dialysis patients.

Challenges in fluid management:

- Narrow window of fluid tolerance: Patients with CKD have limited fluid tolerance. Frequent assessments of the haemodynamic state and frequent fluid regime adjustments are mandatory. In case of CKD fluid should be given considering 50% of normal fluid calculation.
- Urine output: The urine output should not be used as an indicator of the intravascular volume status because patients with CKD can have either low or high urine-output renal failure. Low urine output in CKD contributes to the risk of fluid overload whereas high urine output may aggravate hypovolaemia.
- Limited effect of diuretics: Diuretics have a limited effect in CKD, making patients more susceptible to fluid overload. Dialysis may be required.
- Patient on MHD preferably dialysis session should be deferred.

Acid base balance and electrolyte balance:

Patients with CKD are at risk of metabolic acidosis and electrolyte imbalance which will become worse during dengue shock. If these persist after adequate fluid replacement, dialysis may be considered after haemodynamic stability is achieved.

Platelet dysfunction:

Platelet dysfunction, well recognized in CKD together with severe thrombocytopenia with or without coagulopathy, predispose the dengue patient to severe bleeding that may be difficult to control.

Chronic heart disease with or without heart failure:

- Congenital or acquired cardiac lesions such as valvular heart disease or ischaemic heart disease, especially the later, are common co-morbidities in adults or the elderly.
- In dengue with high fever, tachycardia and increased metabolic demands may precipitate decompensation of cardiac functions.
- Such patients have limited ability to compensate for hypovolaemia or hypervolaemia.
- Fluid therapy should be guided by frequent clinical assessments, haematocrit and blood gas determinations.
- Patients with cyanotic heart diseases have polycythemia and a high baseline haematocrit.
- Non-invasive positive pressure ventilation should be considered to support patients with cardiac decomposition. Failing this, mechanical ventilation should be instituted.
- Loop diuretics should be used cautiously and in a timely way: after achieving haemodynamic stability when intravenous fluid therapy has been discontinued or reduced and in patients with fluid overload.

Ischemic Heart Disease:

- Aspirin/clopidogrel should be avoided for certain days (3-4 days), until the patient recovers from DHF.
- Patients with IHD are more prone to cardiac dysrhythmia, cardiac failure and thrombo-embolism.

Hypertension Interpretation of BP:

- Hypotension is a late sign of shock. However, in patients with uncontrolled hypertension a BP reading that is considered normal for age may, in reality, be low for patients with uncontrolled hypertension.
- What is considered as “mild” hypotension may in fact be profound.
- Patients with chronic hypertension should be considered to be hypotensive when the mean arterial pressure (MAP) declines by 40 mmHg from the baseline, even if it still exceeds 60 mmHg. (For example, if the baseline MAP is 110 mmHg, a MAP reading of 65 mmHg should be considered as significant hypotension).
- Look for other manifestations of shock.

Management Issue:

- ß-blockers, a common antihypertensive medication, cause bradycardia and may block the tachycardic response in shock. The heart rate should not be used as an assessment of perfusion in patients on ß-blockers.
- Antihypertensive agents such as calcium channel blockers may cause tachycardia. Tachycardia in these patients may not indicate hypovolemia.
- Knowing the baseline heart rate before the dengue illness is helpful in the haemodynamic assessment.

The Impact on Hypotension:

- The continuation of antihypertensive agents during the acute dengue illness should be evaluated carefully during the plasma leaking phase.
- The BP lowering effects of these agents and diuretic therapy may exacerbate the hypotension and hypoperfusion of intravascular volume depletion.

Diabetes Mellitus: Diabetes with Dengue:

Type-2 diabetes (T-2 DM) is an independent risk factor for progressing to DSS or severe dengue. T-2 DM patient irrespective of co morbidities are higher risk of develop in DHF/DSS/ severe dengue.
Diabetes with dengue is considered as dengue with comorbid condition. So, they should be managed in hospital for close monitoring.
Oral antidiabetic agents should be avoided as they aggravate GI upsets and risk of hypoglycemia. Dengue itself aggravate hyperglycemia may leads to ketoacidosis or hyperglycemic hyperosmolar state.
So preferred treatment option is insulin with basal-bolus regimen. If dengue haemorrhagic fever or with warning sign then should start intravenous insulin with validated protocol. Target glucose level of & lt; 150 mg/dl should be used.
Monitoring should be done every 1-2 hour until glucose value become stable then every 4 Hours

- Hyperglycaemia results in osmotic diuresis and worsens intravascular hypovolaemia.
- Not correcting the hyperglycaemic state exacerbates the shock state
- Hyperglycaemia also puts patients at risk of bacterial infection.

Diabetic ketoacidosis and hyperosmolar hyperglycaemia:

- Clinical manifestations of diabetic ketoacidosis and hyperosmolar hyperglycaemia (nausea, vomiting and abdominal pain) are similar to the warning signs of severe dengue.
- It is not uncommon for dengue shock to be misdiagnosed as diabetic ketoacidosis.

Hypoglycaemia:

- Hypoglycaemia may occur in those patients taking oral hypoglycaemic gents (e.g. long-acting sulphonylurea), but who had poor oral intake.
- Hypoglycaemia could be aggravated by severe hepatitis from dengue.
- Oral hypoglycaemic agents: Gastrointestinal absorption of oral hypoglycaemic agents is unreliable because of vomiting and diarrhoea during the dengue illness.
- Some hypoglycaemic agents such as metformin may aggravate lactic acidosis, particularly in dengue shock. These agents should be avoided or discontinued during dengue shock and also in those with severe hepatitis.

Management:

- Dengue patients with known diabetes mellitus should be admitted for closer monitoring of the diabetic as well as dengue states.
- If the patient has gastrointestinal disturbances, blood glucose should be controlled with intravenous short-acting insulin during the dengue illness.
- A validated protocol for insulin dose adjustments to a target glucose level of < 150 mg/dl (8.3 mmol/L) should be used.
- A source of glucose may be maintained once the target is achieved while receiving intravenous insulin.
- Blood glucose should be monitored every 1–2 hours until glucose values and insulin rates are stable and then every 4 hours thereafter.

Patient on Steroid Therapy for Other Condition:

In this situation steroid should not be abruptly stopped. But, if necessary, equivalent dosage may be given per IV route during the treatment period.

- Avoid sudden withdraw of steroid.
- According to patient clinical condition may need stress dose of steroid (double or triple of physiological dose) or even intravenous hydrocortisone.

Patient with Malignancy:

- Stop chemo-therapy and radiotherapy should be stop immediately
- Treat Dengue fever according to the national guideline
- After complete recovery patient should be referred to the oncology department.

Fluid Hypersensitivity and Anaphylaxis:

High flow rate of fluid of room temperature may cause shivering, that needs fluid to be warmed up to near body temperature to avoid that which may create discomfort and terrorize the patient or attendant and jeopardize the management as well. In some instances, hypersensitivity or anaphylaxis may occur for which immediate standard treatment of hypersensitivity and anaphylaxis should be instituted.

General Rules:

In these special situations or other upcoming similar unforeseen conditions not experienced before the following general rule may be adopted:

- Assessment and management by risk versus gain approach
- Frequent consultations with peers of relevant specialties
- If necessary multidisciplinary team management
- Patient should be hospitalized under close monitoring
- Searching for references and evidence of similar conditions
- Keep document and arrange for dissemination, publication or communication.

PEARLs:

Some PEARLs may help for taking some spot decision, these are:

- Leukocyte count has a very important prognostic guide in early phase of d e n g u e infection. Leucopenia < 5000 cells/mm3 indicates that within the next 24 hours the patient will have no fever and he will be entering the critical phase.
- What should not be done is as important as what should be done and what should be done should not be overdone.
- Haemorrhage during febrile phase signifies DF with unusual haemorrhage and possibly not DHF. But haemorrhage without fever should be critically assessed for DHF.
- Multiplying Hb level by 3 is usually found to be around the Hct level.
- Sudden pallor signifies internal bleeding.
- When Hct cannot be done or is not available the following clinical tips may help to speculate in DHF setting:
    - If the patient has/ had deep/massive bleeding from gut or other sites the possibility is that the patient may have lower Hct because of blood loss.
    - If the patient has/had surface/mild bleeding the possibility is that the patient may have higher Hct.
    - Sudden unexplained deterioration of haemodynamic status and or refractory to adequate fluid therapy the possibility is more of blood loss and hence low Hct level.
- In any complicated situation frequent consultations with other colleagues and multi-disciplinary team approach are useful.

Guidelines for managing dengue patients in the Intensive Care Unit (ICU)

Chapter-9

Guidelines for managing dengue patients in the Intensive Care Unit (ICU)

Dengue infection can result in severe clinical manifestations requiring intensive care. Effective triage is critical for early clinical management to reduce morbidity and mortality. The percentage of dengue patients who require intensive care unit (ICU) admission is generally low, between 0.1% and 9%.

9.1 Indications for HDU/ ICU Admission:

Criteria of Dengue patients to be shifted in HDU/ICU:

a) Profound shock in spite of all inpatient management fails.
b) Severe metabolic abnormalities (metabolic acidosis, severe hypocalcemia, severe hyponatremia, severe hypoglycemia).
c) Multi-organ impairment - hepatic failure, renal failure, myocarditis, encephalopathy, pancreatitis (at least 2 organs failure or more).
d) DIC with uncontrolled bleeding

Multi-organ impairment	**Criteria**
Hepatic failure	Prothrombin Time >50 secs (or INR >3.5)
Renal impairment	Serum creatinine >300 mmol or 3.38 mg/dl; or anuria.
Myocarditis, cardiomyopathy and MI	Clinical correlation plus ECG and enzyme change
Encephalopathy	Grade 3 (marked delirium, drowsy, sleepy but responds to pain and voice, gross disorientation) or Grade 4 encephalopathy (unresponsive to voice, may or may not respond to painful stimuli, unconsciousness).
Pancreatitis	Clinical correlation plus raised amylase or lipase
Severe metabolic abnormalities	
Metabolic acidosis	pH <7.25 or bicarbonate <15mmol/litre after 2 crystalloid boluses and 1 colloid bolus.
Severe hypocalcaemia or severe hyponatremia or severe hypoglycaemia	Severe hypoglycaemia - <70 mg/dl or <3.9 mmol/L Severe hyponatremia - <124 mmol/L Severe hypocalcaemia - <2.1 mmol/L or <8.5 mg/dl
DIC with uncontrolled bleeding	• Presence of dengue shock syndrome – Essential • Platelets ($x10^9$/L): >100 = 0, <100 = 1, <50 = 2 • Highly elevated FDP or D-dimer: No increase = 0, Moderate = 2, strong = 3 • Prolonged prothrombin time: <3 sec = 0, >3 sec but <6 sec = 1, >6 sec = 2 • Fibrinogen: >1 gm/L = 0, <1gm/L = 1 **Total score:** ≥5 = compatible with overt DIC <5 = repeat monitoring over 1-2 days

9.2 ICU Management Considerations:

Monitor Vital Signs Continuously:

- Heart rate, blood pressure, respiratory rate, oxygen saturation.
- Inferior vena cava (IVC) collapsibility index (IVC-CI) or Central venous pressure (CVP), if indicated.

Fluid Management:

- Balanced fluid resuscitation to manage plasma leakage (According to DSS flow chart).
- Avoid fluid overload (monitor for signs of pulmonary edema).

Haemodynamic Monitoring:

- Maintain mean arterial pressure (MAP)≥ 65mm Hg and urine output ≥ 0.5ml/kg/hour.
- If patient is in septic shock, give fluid 30ml/kg body weight.
- If mean arterial pressure (MAP) is not maintained, start inotropes and vasopressor.
- Noradrenaline: Septic shock (Dose: 0.01–3 mcg/kg/min)
- Vasopressin: along with noradrenaline in septic shock. (Dose: 0.01–0.04 U/min).
- Dobutamine: In cardiogenic shock (myocarditis, ischemic heart disease).

Haemorrhagic Complications:

- Transfuse platelets
- Transfuse fresh frozen plasma (FFP) for coagulopathy or disseminated intravascular coagulation (DIC).

Supportive Care:

- Mechanical ventilation for respiratory failure
- Renal replacement therapy (RRT) for acute kidney injury (AKI).
- Blood products for coagulopathy or blood for severe anemia.
- Neurological manifestations like encephalopathy.

Modes of Ventilatory Support:

a) Non-Invasive Ventilation (NIV): Early intervention with CPAP or BiPAP can help stabilize respiratory effort in patients who are co-operative and haemodynamically stable
b) Invasive ventilation (mechanical ventilation).

9.3 Indication of mechanical ventilation in dengue patients:

a) Severe Respiratory Failure
   - Acute Respiratory Distress Syndrome (ARDS).
   - Hypoxemia (PaO_2 < 60 mmHg on high-flow oxygen) or hypercapnia ($PaCO_2$ >50 mmHg) with respiratory acidosis.
   - Persistent respiratory rate >35 breaths/min with fatigue of respiratory muscle or impending respiratory arrest.

b) Severe Shock (Dengue Shock Syndrome)
   - Hypotension unresponsive to aggressive fluid resuscitation, leading to compromised oxygen delivery.
   - Multi-organ dysfunction with signs of inadequate tissue perfusion (e.g., lactate > 4 mmol/L, anuria).

c) Severe haemorhage
   - Massive gastrointestinal bleeding or hemoptysis causing airway compromise.

d) Neurological complications
   - Encephalopathy or seizures leading to loss of airway protective reflexes.
   - Raised intracranial pressure with compromised ventilation.

Lung-Protective Strategy in patient with ARDS:

- Tidal volume: 4–6 mL/kg of ideal body weight.
- Plateau pressure: <30 cm H_2O.
- PEEP: Adjust based on oxygenation needs.
- Oxygen targets: SpO_2 > 92%, avoiding hyperoxia.
- Consider prone positioning in severe ARDS.

Prevention of Ventilator-Associated Complications:

Ventilator-Associated Pneumonia (VAP):

- Implement strict infection control measures.
- Regular oral hygiene with chlorhexidine.
- Elevate the head of the bed to 30–45°.
- Early weaning from ventilatory support when the patient is stable.

Monitoring and follow-up of ventilated patient:

- Regular ABG analysis to monitor oxygenation and ventilation.
- Daily assessment of ventilator settings.
- Begin weaning when the patient shows clinical improvement.

9.4 Investigations in HDU/ICU:

- Complete blood count (CBC)
- Blood glucose
- Blood gas analysis (Venous blood sample is preferred)
- Blood lactate
- Blood urea, serum electrolytes and serum creatinine, calcium, magnesium
- Liver function tests
- Coagulation profile (PT, APTT, INR)
- Chest radiograph
- ABO blood grouping and Rh typing.
- Cardiac enzymes or ECG if indicated, especially in adults
- Serum amylase, lipase and ultrasound if abdominal pain does not resolve with fluid therapy
- Any other test, if clinically indicated.

9.5 Weaning Criteria for Mechanical Ventilation in Dengue Patients

Weaning from mechanical ventilation should be gradual and carefully monitored.

a) Resolution of primary cause
   - Improvement or resolution of ARDS.
   - Control of bleeding and correction of coagulopathy.

b) Stable Haemodynamic Parameters
   - No vasopressor requirement or minimal vasopressor support needed
   - Adequate perfusion with normal lactate levels and urine output (>0.5 mL/kg/hour)

c) Adequate Oxygenation
   - PaO_2 >60 mmHg on FiO_2 ≤40% with a PEEP ≤5 cmH_2O.
   - SpO_2 >92% on minimal ventilatory support.

d) Adequate Respiratory Mechanics
   - Tidal volume >5 mL/kg predicted body weight.
   - Respiratory rate <30 breaths per minute with adequate spontaneous effort.

e) Neurological Stability
   - Alert or easily arousable with intact airway protective reflexes.

9.6 Spontaneous breathing trial (SBT):

SBT is a period during which a patient breathes with minimal or no assistance from the ventilator to assess their ability to sustain spontaneous breathing. It is typically performed using modes like T-piece breathing, CPAP, or Pressure Support Ventilation (PSV).

Features of successful spontaneous breathing trial:

- Patient able to breathe spontaneously on minimal ventilator settings for 30-120 minutes without signs of distress.
- No significant tachypnea or use of accessory muscles.
- Stable heart rate and blood pressure.
- No signs of fatigue or respiratory acidosis.

Post-Weaning Monitoring:

- Continuous monitoring of respiratory rate, oxygenation, and signs of respiratory distress.
- Early detection of criteria for reintubation, such as respiratory failure or airway compromise.

9.7 Criteria for Discharge of Dengue Patients from ICU:

a) Haemodynamic Stability
- Resolution of shock
- Stable blood pressure (MAP ≥ 65 mmHg) without vasopressors.
- Adequate capillary refill and no signs of hypoperfusion.
- Normal heart rate.

b) Resolution of Plasma Leakage
- Decreased need for intravenous fluids.
- Haematocrit normalization.
- Absence of pleural effusion or ascites on clinical or ultrasound examination.

c) Control of haemorrhage
- No active bleeding for at least 24-48 hours.
- Normal or stabilized platelet count (≥50,000/mm^3 is often preferred).
- No requirement for ongoing blood product transfusion.

d) Normalization of Organ Function
- Renal function: Adequate urine output (>0.5 mL/kg/hour) without renal replacement therapy.
- Liver function: No signs of hepatic encephalopathy or significant coagulopathy.
- Neurological status: Alert and oriented, with resolution of encephalopathy or seizures.

e) Resolution of Respiratory Distress
- Stable oxygenation with room air or minimal supplemental oxygen.
- No signs of respiratory distress or impending respiratory failure.

f) Laboratory Stability
- Hematological parameters: Stable haematocrit and platelet count.
- Electrolytes and acid-base balance within normal ranges.

g) General Well-being
- Ability to tolerate oral intake, with improved appetite and hydration.
- No significant pain, discomfort, or other complications requiring ICU-level care.

Community Engagement and Prevention

Chapter-10

Preventive and control measures at various levels, the following actions may be taken:

10.1 Household:

Intensifying efforts to reduce larval habitats in and around houses by covering all water storage containers in the house to prevent egg-laying by mosquito, and emptying, drying water tanks, containers, coolers, birdbaths, pets' water bowls, plant pots and drip trays at least once every week.

- Discard all waste articles, tyres, etc. that are lying in open and may hold water during rains. Tyres should be properly disposed. If there is no proper disposal system, it may be buried under the ground, though it is not an ideal disposal system, as it may releases chemicals, pollute water and soil, thereby creating an environmental hazard
- Check for gutters and flat roofs regularly for any clogging and water stagnation
- Carry out spray with commercially available safe aerosols (Pyrethroid-based)
- Rooms including closets and kitchens should be sprayed (by removing/covering all food items properly). Room may be closed for 15–20 min for effective results and time of spray should coincide with biting time of the *Ae. aegypti* mosquito, e.g., early morning or late afternoon.
- Take personal protection measures, i.e., protective clothing (full sleeved shirts and full pants during day time), and using commercially available repellents
- Use insecticide-treated mosquito nets while sleeping during day time
- Ensure doors and windows have screens/wire mesh
- Larvivorous fishes (e.g., Gambusia/Guppy) may be introduced in ornamental water tanks/garden
- Pass the message on preventive measures to different peer groups.

10.2 Community:

Activities may be under taken by different groups, i.e., resident welfare associations (RWAs), nongovernmental organizations (NGOs), self-help groups (SHGs), and faith-based organizations (FBOs). These groups should reinforce the house-hold measures in larger aspects and launch campaigns in raising awareness. The awareness campaigns should include common signs and symptoms of *Aedes*-transmitted arboviral diseases, warning signs, home care, preventive and control measures.

Some of the activities are as follows:

- Ensure all overhead water storage tanks have well-fitted lids and overflow pipe has a wire mesh to prevent the entry of mosquito.
- Create awareness among local residents to observe dry day ever week and follow all measures suggested under household level.
- These groups can identify construction sites and advice the builder/contractor on the need for taking antilarval measures at these sites.
- The groups may volunteer and undertake special campaigns at places of historical importance or of tourist attractions.
- Community groups may carry out cleaning and covering water storage containers.
- Keeping the surroundings clean and organising sanitation measures.

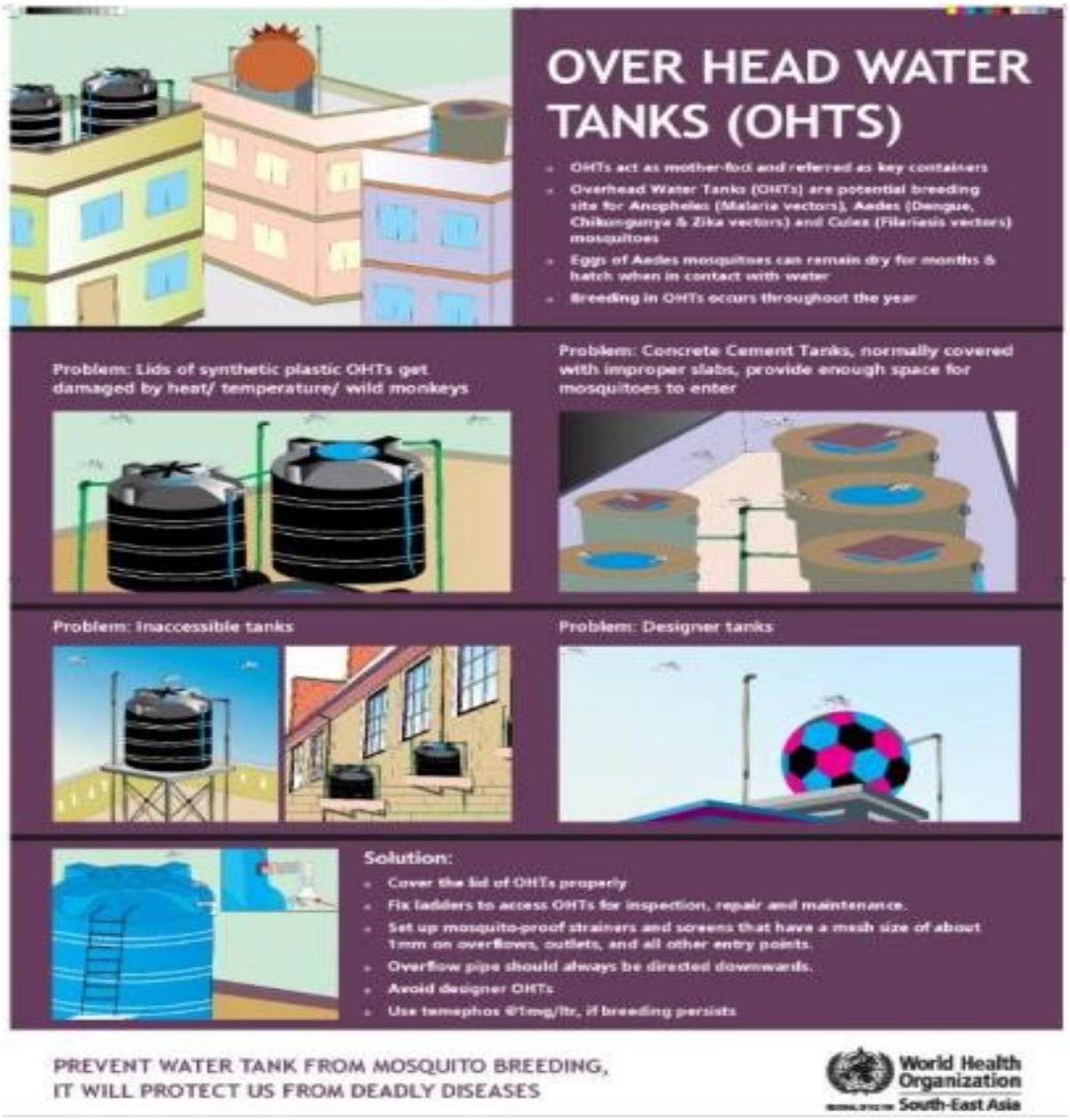
- Carry out cleaning weeds and tall grass to reduce resting places for adult mosquitoes.
- Promoting use of mosquito nets to protect infants and small children from mosquito bites during day time.
- Coordinating and participating with local health authorities in organizing camps for insecticide treatment of community owned mosquito nets/curtains.
- In case water containers cannot be emptied, coordination with the health authorities
- for application of temephos granules (1 ppm).
- Mobilize households to cooperate during spraying/fogging.

10.3 Institutions (Hospitals, schools, colleges, other institutions, offices, etc.)

- Designating a nodal officer and his/her team to check every week for *Aedes* larval habitats inside the premises, i.e., overhead tanks, ground water storage tanks, air coolers, planters, flower pots, etc.
- Ensuring source reduction by covering all water tanks with mosquito proof lids.
- Emptying, drying water containers, coolers, plant pots at least once each week.
- Checking for clogged gutters and flat roofs for any water accumulation.
- Introducing larvivorous fishes (e.g., Gambusia/Guppy) in ornamental water tanks/garden.
- Carrying out indoor space spraying with pyrethrum 2% or cyphenothrin, etc.
- Promoting personal protection measures.
- Putting tight-fitting screens/wire mesh on doors/windows.
- Reporting all fever cases (suspected dengue) to local health authorities.


CONSTRUCTION SITES
Water collection can occur in all available artificial containers at construction sites
Disease transmitting mosquitoes reproduce freely in these containers
Construction workers and nearby communities are exposed to these mosquitoes and therefore suffer from Vector Borne Diseases
Problem: Stagnant water in equipment and machinery
Solution: Apply one of these on weekly basis
Problem: Water stored in containers like curing tanks, drums, etc.
Solution: Apply one of these
Cover all containers
Store under shelter
Problem: Water collection in lift shaft areas, pits, tarpaulin, temporary drainage etc.
Solution: Apply whichever applicable
Place tarpulin without grooves
Clean drainage weekly
Problem: Debris, Discarded items and Receptacles holding water
Solution:
CONTRACTOR IS PRIMARILY RESPONSIBLE TO CONTROL MOSQUITO BREEDING AT THE CONSTRUCTION SITE IN CONSULTATION WITH PUBLIC HEALTH DEPARTMENT
World Health Organization
South-East Asia


DOMESTIC BREEDING SITES
A number of potential mosquito breeding sites exists in a house
Few of these containers hold water throughout the year and support breeding of Aedes
These containers act as mother-foci and referred as key containers
During transmission season, Aedes spread from key containers to seasonal containers and transmit disease(s)
Problem: Water stagnation on the roof of the house
Solution:
Problem: Water storage in underground water storage tanks and containers
Solution:
Problem: Water collection in artificial fountains, bird pots, flower pots
Solution:
Problem: Other containers
Solution:
COMMUNITY SHOULD DEVOTE 1 HOUR IN A WEEK
TO CLEAN AND SCRUB ALL DOMESTIC BREEDING SITES
World Health Organization
South-East Asia


OVER HEAD WATER TANKS (OHTS)
OHTs act as mother-foci and referred as key containers
Overhead Water Tanks (OHTs) are potential breeding site for Anopheles (Malaria vectors), Aedes (Dengue, Chikungunya & Zika vectors) and Culex (Filariasis vectors) mosquitoes
Eggs of Aedes mosquitoes can remain dry for months & hatch when in contact with water
Breeding in OHTs occurs throughout the year
Problem: Lids of synthetic plastic OHTs get damaged by heat/ temperature/ wild monkeys
Problem: Concrete Cement Tanks, normally covered with improper slabs, provide enough space for mosquitoes to enter
Problem: Inaccessible tanks
Problem: Designer tanks
Solution:
Cover the lid of OHTs properly
Fix ladders to access OHTs for inspection, repair and maintenance.
Set up mosquito-proof strainers and screens that have a mesh size of about 1mm on overflows, outlets, and all other entry points.
Overflow pipe should always be directed downwards.
Avoid designer OHTs
Use temephos @1mg/ltr, if breeding persists
PREVENT WATER TANK FROM MOSQUITO BREEDING,
IT WILL PROTECT US FROM DEADLY DISEASES
World Health Organization
South-East Asia

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COMMUNITY/RWA SHOULD ADOPT NEIGHBOURHOOD PUBLIC PLACES AND DEVOTE 1 HR/WEEK TO CLEAN, SCRUB AND REMOVE BREEDING SITES AROUND THE HOUSE

World Health Organization
South-East Asia

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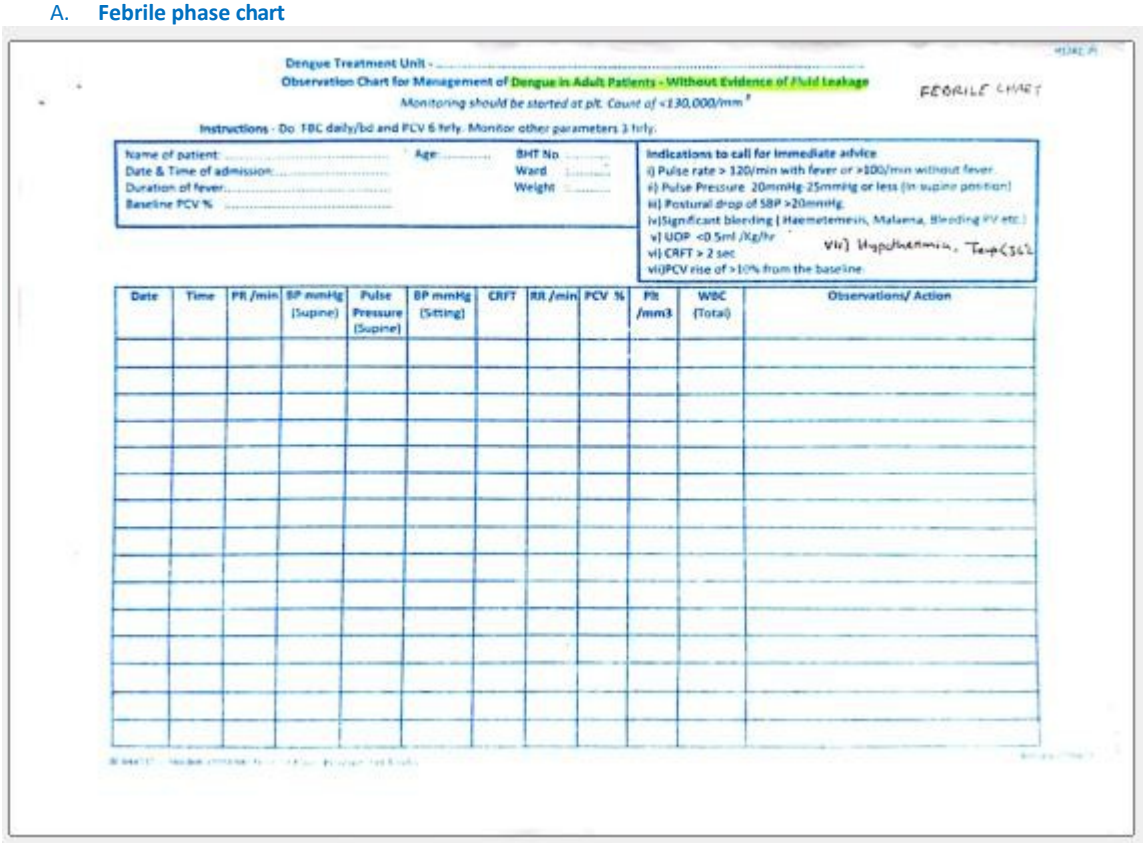
Annexures:

A. **Febrile phase chart**



Dengue Treatment Unit - .....

Observation Chart for Management of Dengue in Adult Patients - Without Evidence of Fluid Leakage

FEBRILE CHART

Monitoring should be started at plt. Count of <130,000/mm³

Instructions - Do TBC daily/bd and PCV 6 hrly. Monitor other parameters 3 hrly.

Name of patient: ..... Age: ..... BHT No .....
Date & Time of admission: ..... Ward .....
Duration of fever: ..... Weight .....
Baseline PCV % .....

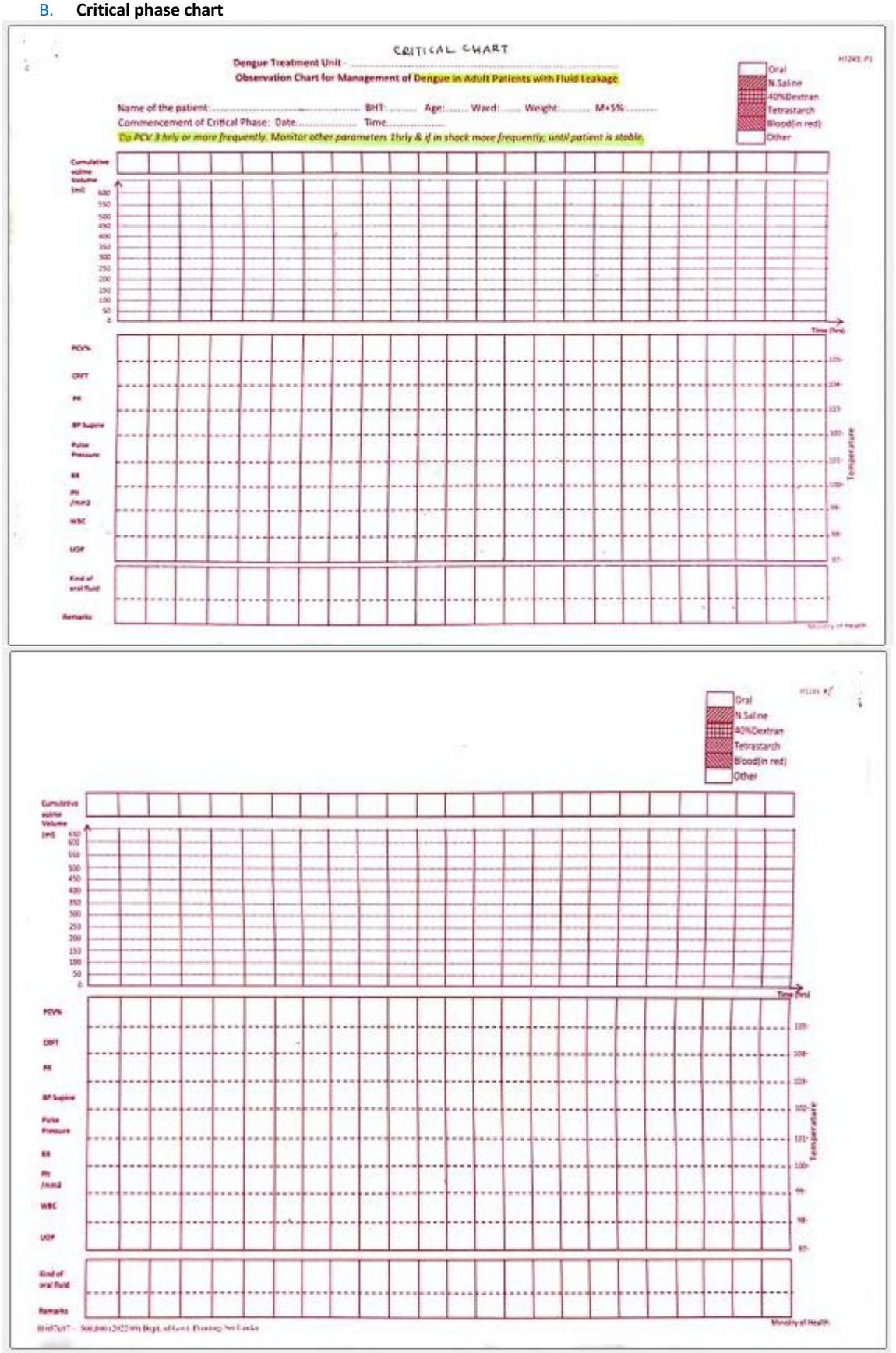
Indications to call for immediate advice
i) Pulse rate > 120/min with fever or >100/min without fever
ii) Pulse Pressure 20mmHg-25mmHg or less (in supine position)
iii) Postural drop of SBP >20mmHg
iv) Significant bleeding (Haemetemesis, Malaena, Bleeding PV etc.)
v) UOP <0.5ml /Kg/hr
vi) CRFT > 2 sec
vii) Hypothermia, Temp<36C
vii)PCV rise of >10% from the baseline

Date	Time	PR /min	BP mmHg (Supine)	Pulse Pressure (Supine)	BP mmHg (Sitting)	CRFT	RR /min	PCV %	Plt /mm3	WBC (Total)	Observations/ Action

Date	Time	PR /min	BP mmHg (Supine)	Pulse Pressure (Supine)	BP mmHg (Sitting)	CRFT	RR (pm)	PCV %	Plt /mm3	WBC (Total)	Observations/ Action

Ministry of Health

B. **Critical phase chart**



C. Pediatric and adolescent febrile chart

Health Form : H-1242A

Monitoring Chart I - for Management of Dengue in Paediatric and Adolescent Patients - Febrile Phase
Patient to be monitored 3 - 6 hourly

Name of the Patient .....BHT.....Date and time of admission.....Ward.....

Duration of Fever.....

Date time	HR/ min (pulse)	BP mmHg	Pulse Pressure	CRFT <2s/ >2s	Extremity Warm/ Cold	RR	Input (ml) Oral/ IV	UOP/ day Void/ catheter	UOP ml/ kg/ hr	Platelet Count 10^3	HCT	Treatment/ Remarks

D. Paediatric and adolescent critical phase chart

Health Form : H-1243A

Monitoring Chart II for Management of DHF in Paediatric and Adolescent Patients during
Critical Phase Patient to be monitored hourly

Name of the Patient.....BHT.....Date and time of admission.....Ward.....

Weight -	Height -	Ideal body weight -	M -	M + 5% = ml

Critical Phase Commencing date and time ..... **End date and time** .....

Fluid ml/kg/hr																							
10																							
9																							
8																							
7																							
6																							
5																							
4																							
3																							
2																							
1.5																							
1																							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Remaining fluid quota																							
HCT																							
HR																							
BP																							
Pulse Pressure																							
RR																							
CRFT																							
Extremities warm/cold																							
UOP void/ catheter																							
UOP ml/Kg/hr																							
Platelet count																							

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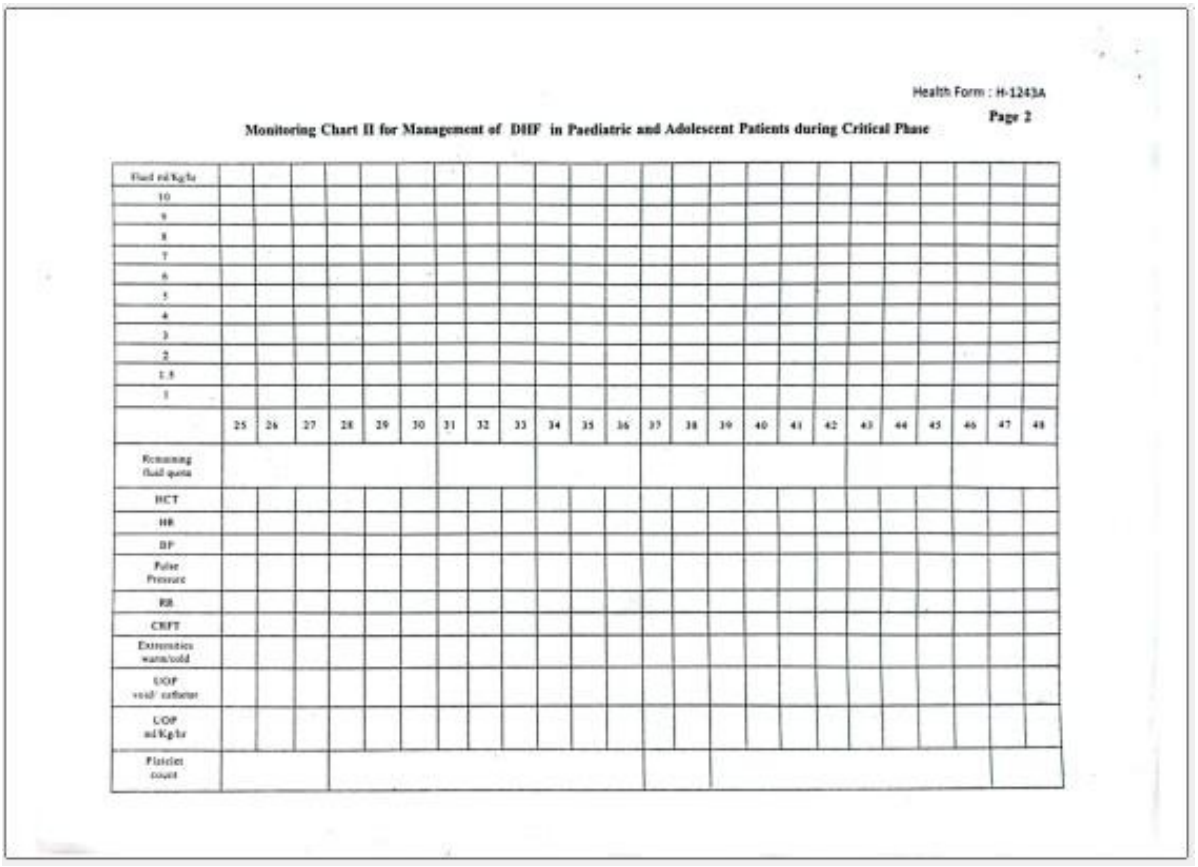


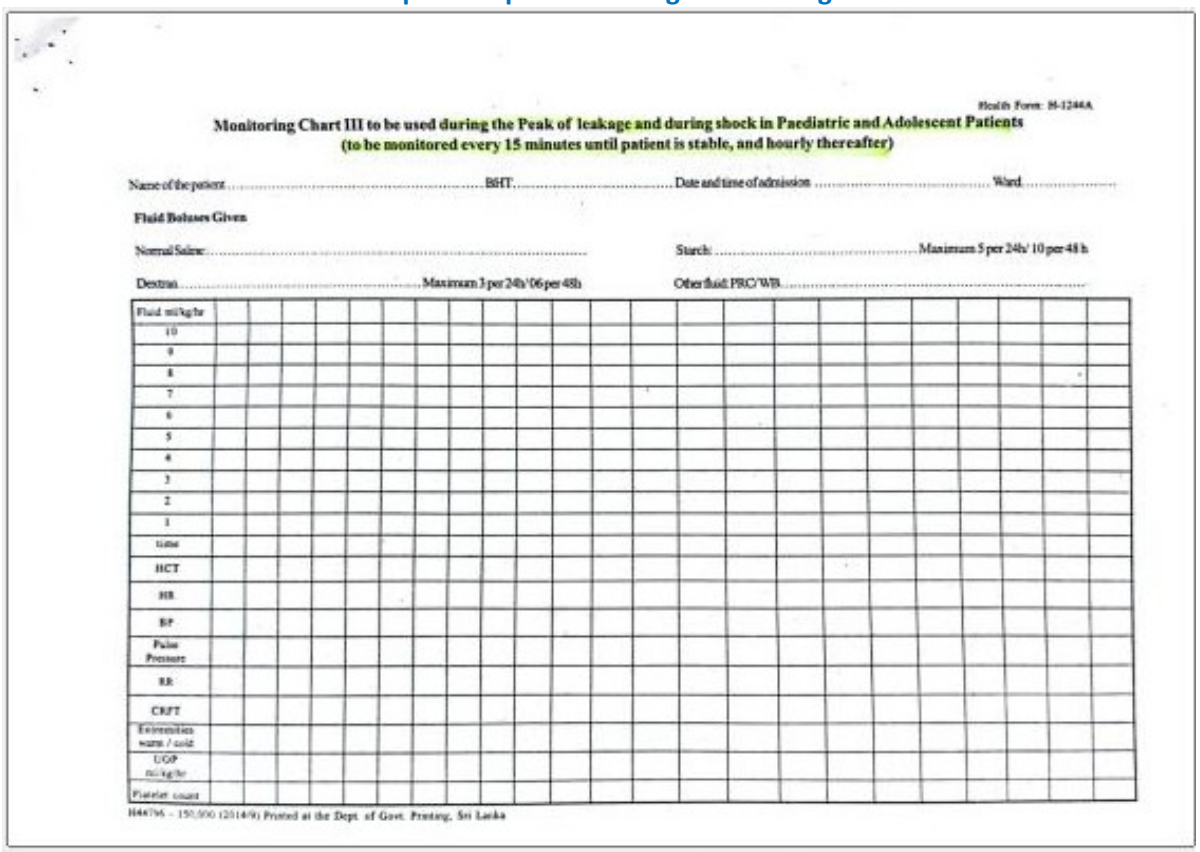
Health Form : H-1243A

Page 2

Monitoring Chart II for Management of DHF in Paediatric and Adolescent Patients during Critical Phase

Fluid ml/kg/hr																							
10																							
9																							
8																							
7																							
6																							
5																							
4																							
3																							
2																							
1.5																							
1																							
	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
Remaining fluid quota																								
HCT																								
HR																								
BP																								
Pulse Pressure																								
RR																								
CRFT																								
Extremities warm/cold																								
UOP void/ catheter																								
UOP ml/Kg/hr																								
Platelet count																								

E. Pediatric and adolescent patient: peak of leakage and during shock.



Health Form: H-1244A

Monitoring Chart III to be used during the Peak of leakage and during shock in Paediatric and Adolescent Patients
(to be monitored every 15 minutes until patient is stable, and hourly thereafter)

Name of the patient ..... BHT: ..... Date and time of admission ..... Ward .....

Fluid Boluses Given

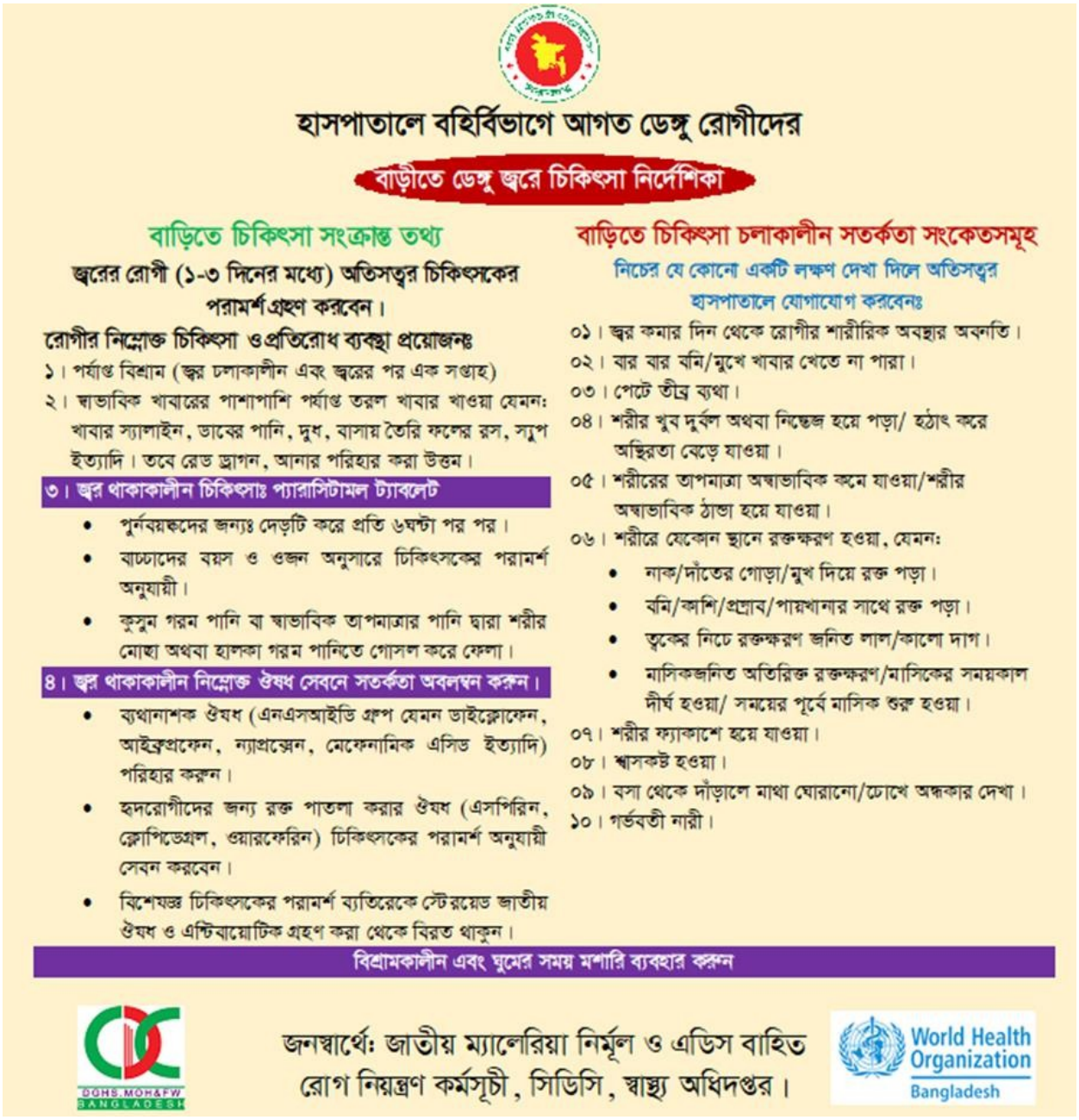
Normal Saline: ..... Starch: ..... Maximum 5 per 24h/ 10 per 48 h

Dextran ..... Maximum 3 per 24h/ 06 per 48h Other fluid: PRC/ WB .....

Fluid ml/kg/hr																							
10																							
9																							
8																							
7																							
6																							
5																							
4																							
3																							
2																							
1																							
Urine																							
HCT																							
HR																							
BP																							
Pulse Pressure																							
RR																							
CRFT																							
Extremities warm / cold																							
UOP ml/kg/hr																							
Platelet count																							

H44796 – 150,000 (2014/9) Printed at the Dept. of Govt. Printing, Sri Lanka

F. Leaflet of Dengue patient home management (in Bangla)



হাসপাতালে বহির্বিভাগে আগত ডেঙ্গু রোগীদের

বাড়ীতে ডেঙ্গু জ্বরে চিকিৎসা নির্দেশিকা

বাড়িতে চিকিৎসা সংক্রান্ত তথ্য

জ্বরের রোগী (১-৩ দিনের মধ্যে) অতিসত্বর চিকিৎসকের পরামর্শ গ্রহণ করবেন।

রোগীর নিম্নোক্ত চিকিৎসা ও প্রতিরোধ ব্যবস্থা প্রয়োজনঃ

১। পর্যাপ্ত বিশ্রাম (জ্বর চলাকালীন এবং জ্বরের পর এক সপ্তাহ)

২। স্বাভাবিক খাবারের পাশাপাশি পর্যাপ্ত তরল খাবার খাওয়া যেমনঃ খাবার স্যালাইন, ডাবের পানি, দুধ, বাসায় তৈরি ফলের রস, স্যুপ ইত্যাদি। তবে রেড ড্রাগন, আনার পরিহার করা উত্তম।

৩। জ্বর থাকাকালীন চিকিৎসাঃ প্যারাসিটামল ট্যাবলেট

- পুর্নবয়স্কদের জন্যঃ দেড়টি করে প্রতি ৬ঘন্টা পর পর।
- বাচ্চাদের বয়স ও ওজন অনুসারে চিকিৎসকের পরামর্শ অনুযায়ী।
- কুসুম গরম পানি বা স্বাভাবিক তাপমাত্রার পানি দ্বারা শরীর মোছা অথবা হালকা গরম পানিতে গোসল করে ফেলা।

৪। জ্বর থাকাকালীন নিম্নোক্ত ঔষধ সেবনে সতর্কতা অবলম্বন করুন।

- ব্যথানাশক ঔষধ (এনএসআইডি গ্রুপ যেমন ডাইক্লোফেন, আইবুপ্রফেন, ন্যাপ্রক্সেন, মেফেনামিক এসিড ইত্যাদি) পরিহার করুন।
- হৃদরোগীদের জন্য রক্ত পাতলা করার ঔষধ (এসপিরিন, ক্লোপিডেগ্রল, ওয়ারফেরিন) চিকিৎসকের পরামর্শ অনুযায়ী সেবন করবেন।
- বিশেষজ্ঞ চিকিৎসকের পরামর্শ ব্যতিরেকে স্টেরয়েড জাতীয় ঔষধ ও এন্টিবায়োটিক গ্রহণ করা থেকে বিরত থাকুন।

বাড়িতে চিকিৎসা চলাকালীন সতর্কতা সংকেতসমূহ

নিচের যে কোনো একটি লক্ষণ দেখা দিলে অতিসত্বর হাসপাতালে যোগাযোগ করবেনঃ

০১। জ্বর কমার দিন থেকে রোগীর শারীরিক অবস্থার অবনতি।

০২। বার বার বমি/মুখে খাবার খেতে না পারা।

০৩। পেটে তীব্র ব্যথা।

০৪। শরীর খুব দুর্বল অথবা নিস্তেজ হয়ে পড়া/ হঠাৎ করে অস্থিরতা বেড়ে যাওয়া।

০৫। শরীরের তাপমাত্রা অস্বাভাবিক কমে যাওয়া/শরীর অস্বাভাবিক ঠান্ডা হয়ে যাওয়া।

০৬। শরীরে যেকোন স্থানে রক্তক্ষরণ হওয়া, যেমনঃ

- নাক/দাঁতের গোড়া/মুখ দিয়ে রক্ত পড়া।
- বমি/কাশি/প্রস্রাব/পায়খানার সাথে রক্ত পড়া।
- ত্বকের নিচে রক্তক্ষরণ জনিত লাল/কালো দাগ।
- নাসিকজনিত অতিরিক্ত রক্তক্ষরণ/নাসিকের সময়কাল দীর্ঘ হওয়া/ সময়ের পূর্বে নাসিক শুরু হওয়া।

০৭। শরীর ফ্যাকাশে হয়ে যাওয়া।

০৮। শ্বাসকষ্ট হওয়া।

০৯। বসা থেকে দাঁড়ালে মাথা ঘোরানো/চোখে অন্ধকার দেখা।

১০। গর্ভবতী নারী।

বিশ্রামকালীন এবং ঘুমের সময় মশারি ব্যবহার করুন

DGHS.MOH&FW BANGLADESH

জনস্বার্থেঃ জাতীয় ম্যালেরিয়া নির্মূল ও এডিস বাহিত রোগ নিয়ন্ত্রণ কর্মসূচী, সিডিসি, স্বাস্থ্য অধিদপ্তর।

World Health Organization Bangladesh

G. Management of complications with their features:

Complications	Feature	Measures
Hepatic failure	Altered mental status, drowsy, disoriented, convulsion, coma Investigation: ALT, AST, s. Bilirubin, PT, S Ammonia..... > increases.	• Adequate fluid therapy and provide nutrition (protein restriction in hepatic encephalopathy). • Hepatic encephalopathy: Lactulose, Rifaximin, L -ornithine L-aspartate (LOLA). • Coagulopathy: FFP, Platelet transfusion, Vitamin K • Hypoglycaemia : IV glucose
Renal failure	Decreased urine output or no urine output.	• Maintain adequate hydration. • Haemodialysis, sustained low-efficiency dialysis (SLED) or continuous renal replacement therapy (CRRT).
Heart Failure	a. Heart Failure with Reduced Ejection Fraction (HFrEF) Feature: EF ≤ 40%. Characterized by impaired left ventricular systolic function.	1. Renin-Angiotensin-Aldosterone System (RAAS) Inhibitors: • ACE Inhibitors (e.g., Enalapril, Lisinopril • ARBs (e.g., Losartan, Valsartan) • ARNI (e.g., Sacubitril/Valsartan) 2. Beta-Blockers: Carvedilol, Bisoprolol, or Metoprolol Succinate 3. Mineralocorticoid Receptor Antagonists (MRA): Spironolactone or Eplerenone 4. SGLT2 Inhibitors: Empagliflozin or Dapagliflozin 5. Diuretics 6. Ivabradine
	b. Heart Failure with Preserved Ejection Fraction (HFpEF) Feature: EF ≥ 50%. Characterized by diastolic dysfunction with normal systolic function.	1. Diuretics 2. Management of Comorbidities: • Hypertension: RAAS inhibitors/ARBs, or MRAs. • Atrial Fibrillation: Anticoagulation and rate/rhythm control. • Diabetes: SGLT2 inhibitors • Coronary Artery Disease: Beta-blockers, nitrates). 3. Mineralocorticoid Receptor Antagonists (MRA): Spironolactone 4. SGLT2 Inhibitors

Heart Failure	a. Heart Failure with Reduced Ejection Fraction (HFrEF) Feature: EF ≤ 40%. Characterized by impaired left ventricular systolic function.	1. Renin-Angiotensin-Aldosterone System (RAAS) Inhibitors: • ACE Inhibitors (e.g., Enalapril, Lisinopril • ARBs (e.g., Losartan, Valsartan) • ARNI (e.g., Sacubitril/Valsartan) 2. Beta-Blockers: Carvedilol, Bisoprolol, or Metoprolol Succinate 3. Mineralocorticoid Receptor Antagonists (MRA): Spironolactone or Eplerenone 4. SGLT2 Inhibitors: Empagliflozin or Dapagliflozin 5. Diuretics 6. Ivabradine
	b. Heart Failure with Preserved Ejection Fraction (HFpEF) Feature: EF ≥ 50%. Characterized by diastolic dysfunction with normal systolic function.	1. Diuretics 2. Management of Comorbidities: • Hypertension: RAAS inhibitors/ARBs, or MRAs. • Atrial Fibrillation: Anticoagulation and rate/rhythm control. • Diabetes: SGLT2 inhibitors • Coronary Artery Disease: Beta-blockers, nitrates). 3. Mineralocorticoid Receptor Antagonists (MRA): Spironolactone 4. SGLT2 Inhibitors
Dengue associated myocarditis, cardiomyopathy and MI	*a. Dengue associated myocarditis:* Chest pain, palpitations, dyspnea, hypotension, and signs of heart failure. • ECG: Arrhythmias, Sinus bradycardia, ST-T wave changes, AV blocks. • Echocardiography: Reduced ejection fraction, global hypokinesis. • Elevated troponin and CK-MB. • Chest X-ray: Cardiomegaly, pulmonary edema. *b. Dengue associated cardiomyopathy:* Acute heart failure, cardiogenic shock. • Elevated jugular venous pressure, pulmonary edema. Echocardiography: Dilated ventricles, reduced ejection fraction. NT-pro BNP: Elevated. *c. Dengue associated MI:* Severe chest pain, dyspnea, hypotension and signs of shock. Diagnosis: • ECG: ST-segment elevation or depression, T-wave inversion. • Elevated troponin and CK-MB. • Echocardiography: Regional wall motion abnormalities.	*a. Dengue associated myocarditis:* • Oxygen Therapy for hypoxemia (mechanical ventilation if needed) • Avoid fluid overload. • Inotropes: Dobutamine or milrinone for low cardiac output. • Anti-arrhythmic: Amiodarone. • Steroids (controversial) Consider in severe cases. *b. Dengue associated cardiomyopathy:* • Diuretics • Noradrenaline • Dobutamine (low CO with poor perfusion) • Avoid fluid overload *c. Dengue associated MI:* • Oxygen Therapy: SpO_2 >92%. • Antiplatelet: Contraindicated • Anticoagulation: Avoid unless platelet count >50,000/mm^3 and no active bleeding. • Thrombolysis: Contraindicated due to high risk of bleeding. • Percutaneous Coronary Intervention (PCI) Preferred (if available and feasible) • Beta-blockers: if there are no signs of heart failure.
Encephalopathy	Drowsy, disoriented, convulsion, coma	• Keep head in midline position. • Elevate the head end of the bed to 30- 45 degrees. • Avoid neck flexion. • 3% NaCl 3-5 ml/kg slow boluses. • Controlled hyperventilation (maintain PaCO2 between 30 to 35 mmHg) • Steroid to reduce ICP. Dexamethasone 0.15

		mg/kg/dose IV to be administered every 6–8 hours.
Pancreatitis	• Abdominal Pain / Severe epigastric pain, radiating to the back. • Nausea and Vomiting 1. Laboratory Investigations: • Serum Amylase and Lipase: Elevated • Liver Function Tests (LFTs): Elevated ALT, AST, and bilirubin. • Serum Calcium: Hypocalcemia • Elevated CRP and leukocytosis. • USG Abdomen: enlarged, inflamed pancreas or peripancreatic fluid. • CT Scan Abdomen: pancreatic inflammation, edema, or necrosis.	• Maintain intravascular volume. • Maintain nutrition • Analgesic (avoid NSAIDs) • Antibiotic • Treatment of complications.
Metabolic acidosis	ABG: Normal or high anion gap metabolic acidosis. P^H decrease PCO_2 decrease HCO_3^- decrease	• $NaHCO_3$ can be considered
Severe hypocalcemia	Tetany	• 10 ml of 10% calcium gluconate over 10 minutes. • Can be repeated every 6 hours if the patient is not improving.
Severe hyponatremia	Altered mental status	• 3% NaCl 3-5ml/kg as a slow IV bolus over 60 minutes through a larger vein
Hypoglycaemia	Shaking or trembling, sweating, faster heart rate, confusion etc.	• Administer 10% dextrose, 2 ml/kg followed by 5% DNS infusion.
Convulsion		• Phenobarbital and diazepam IV as indicated.
DIC with severe bleeding	Bleeding from multiple sites, bruising. Presence of an Essential associated factor Platelet > 100 = 0 < 100 = 1 < 50 = 2 Elevated FDP No increase = 0 Moderate = 2 Strong = 3 Prolonged PT < 3 sec =0 > 3 sec but < 6 sec =1 > 6 sec =1 Fibrinogen > 1 g/L =0 < 1 g/L =1 Total score ≥ 5 =Compatible with overt DIC ≤5 = Repeat monitoring over 1-2 days.	• Transfuse fresh frozen plasma, platelets, freshly packed red cells.
		• Antibiotic

H. Inferior Vena Cava (IVC) Collapsibility Index (IVCCI)

The IVC Collapsibility Index (IVCCI) is a dynamic ultrasound-based measurement used to estimate intravascular volume status and assess fluid responsiveness in critically ill patients. It is especially useful in guiding fluid management in cases of hypovolemia or shock.

Definition:

The IVC-CI is calculated as the percentage change in the diameter of the IVC during the respiratory

cycle.

$$IVC - CI = \frac{(IVC\ diameter\ during\ expiration\ -\ IVC\ diameter\ during\ inspiration)}{IVC\ diameter\ during\ expiration} \times 100$$

Normal Values and Interpretation:

- < 15%: Low collapsibility. Indicates hypervolemia or low fluid responsiveness.
- 15-40%: Intermediate collapsibility. May require further clinical assessment.
- > 40%: High collapsibility. Indicates hypovolemia or high fluid responsiveness.

Procedure:

1. Patient Position: The patient is typically placed in the supine position.
2. Probe Placement: A subxiphoid or transabdominal view is used with a low-frequency ultrasound probe.
3. Measurements: It is measured in M-mode ultrasound at the subxiphoid view just proximal to the hepatic vein.
    - IVC diameter during expiration (IVCe) and inspiration (IVCi).
4. Respiratory Variations: The IVC collapses during inspiration due to negative intrathoracic pressure and expands during expiration.

*** In mechanically ventilated patients, a similar parameter, the distensibility index, is used.