REVIEW ARTICLE

Dengue Fever: In-Hospital Management of Critically ill Adult Patients

Aamir Shahzad[1], Kiran Fatima[2]

ABSTRACT

Dengue is rapidly becoming a major public health problem with significant mortality and morbidity. Management especially in first two days needs careful attention. We present a review of current literature on the management critically ill adult patients of dengue in hospital settings. Early diagnosis and close monitoring of response to treatment are necessary to prevent worse outcomes.

Key Words: *Dengue, Dengue Hemorrhagic Fever, Dengue Shock Syndrome.*

How to cite this: *Shahzad A, Fatima K. Dengue Fever: In-Hospital Management of Critically ill Adult Patients. Life and Science. 2021; 2(2): 66-70. doi: http://doi.org/10.37185/LnS.1.1.93*

Introduction

Dengue (Break bone) fever is one of the rapidly emerging infectious diseases across the globe. Pakistan has also experienced huge outbreaks affecting thousands of people.[1]

Dengue, an arthropod borne virus affects individuals from all age groups. It is mainly spread by mosquitoes Aedes aegypti and Aedes Albopictus during rainy season. As there is no effective anti-viral drug available, case detection, management and vector control are main strategies for its prevention and control.

This review will mainly focus on principles of treatment of critically ill adult patients especially in the first 24-48 hours.

Management

In early phase it is important to recognize clinical and laboratory features of plasma leakage and circulatory shock. 'Red flag' signs are pain/tenderness in abdomen along with persistent vomiting, clinical signs of fluid in pleural/peritoneal cavity, bleeding manifestations, an enlarged tender liver and oliguria. Laboratory features of increase in Hematocrit (HCT) and decrease in platelet counts are important to recognize. Other uncommon manifestations are hepatic failure, myocarditis, and encephalopathy. At times these might be severe and may occur with minimal features of increased capillary permeability.[2,3] Exact management plan varies according to the needs of the patient. However certain basic principles must be kept in mind.

Fluid management

Close attention to fluid balance is important. Unnecessary fluid administration based only on Hematocrit (HCT) level without consideration of clinical condition, prolonged fixed fluid administration without varying the dose according to the rate of plasma leak and continuous intravenous fluid during convalescent phase should be avoided.[4]

Patients in critical phase without shock

In hemodynamically stable patients, in the absence of vomiting; oral fluid administration is sufficient. Intravenous fluids are needed if there is increase in HCT which indicates ongoing capillary leakage, or presence of persistent vomiting or intolerance to oral fluids.[4]

Dengue shock syndrome (DSS): Compensated and decompensated

It is a medical emergency. Early diagnosis and administration of fluid to replace leakage is important step and ensures a good prognosis. Disease outcomes becomes less certain with progression to a decompensated state. Pulse

[1]*Department of Medicine*
National University of Medical Sciences, Rawalpindi
[2]*Department of Medicine*
Islamic International Medical College
Riphah International University, Islamabad

Correspondence:
Dr. Kiran Fatima
Department of Medicine
Islamic International Medical College
Riphah International University, Islamabad
E-mail: kiranfatima07@gmail.com

Funding Source: NIL; Conflict of Interest: NIL
Received: Jan 01, 2020; Revised: Feb 04, 2020
Accepted: Feb 18, 2021

pressure of < 20 mm of Hg and oliguria (less than 600 ml/day) are late signs of shock.[5,6]

Aggressive fluid administration must be started immediately.

Normal saline (0.9%) solutions is sufficient. In case of inadequate response, colloid solutions may be used. During fluid administration, it is important to watch for signs of fluid overload and oral fluids should be given when the patient is able to take orally.[7]

Persistent shock

In case a patient fails to improve despite adequate fluid replacement, a thorough clinical assessment is required to identify and treat following subcategories.

1. Significant bleeding (often occult): Treat with packed cell volume (PCV). In case HCT is more than 45, IV fluids should be given prior to blood transfusion.
2. Hypocalcemia: A slow infusion (over 10 minutes) of 10 % Calcium gluconate should be given as IV bolus at a dose of 1 ml/kg (max 10 ml). It may be repeated hourly if required. In some cases where patients may fail to improver despite adequate fluid replacement, IV calcium may be tried empirically.
3. Acidosis: Intravenous administration of 8.4% $NaHCO_3$ is given if serum HCO_3 fall below 15 mEq/l. It should be given in a dose of 1 ml/kg diluted in equal volume of normal saline in slow infusion.
4. Hypoglycemia: Should be treated with IV glucose (50 ml of 50% glucose solution).

If despite all the above mentioned therapeutic steps, patient fails to recover from shock; sepsis and/or cardiogenic shock as possible aggravating factors. In such cases treatment should be modified to include broad spectrum antibiotics according to local culture/sensitivity recommendations and inotropic support to maintain mean arterial pressure.[4,8]

Management of bleeding and Homeostasis

Superficial and mucosal bleeding along with thrombocytopenia, sometimes falling below the critical level of 20,00/liter is commonly seen in adults in the absence of a precipitating factor or significant plasma leakage.

At times patients may show an increased level of activated partial-thromboplastin time (aPTT) along with decrease in fibrinogen levels. These abnormal values in the presence of thrombocytopenia may suggest DIC (disseminated intravascular coagulation) However, the exact pathophysiology remains unclear.[9,10,11]

Occult bleeding

Bleeding is called significant if it results in hemodynamic instability. It usually occurs on a background of persistent acidosis and/or circulatory shock. Significant bleeding should be suspected there is a mismatch between HCT and the state of shock. (HCT fails to rise in the presence of circulatory shock) or an unexpected fall in HCT without clinical improvement. Similarly, severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement should alert the physician to the possibility of occult bleeding.[12,13]

Superficial mucosal bleeding stops spontaneously without therapy. However significant bleeding should be treated with packed cell volume or with fresh whole blood.

Use of proton pump inhibitors in upper GI bleeding is not based on scientific evidence. In serious cases diagnostic or therapeutic endoscopic procedures are not safe. They may further increase the risk of bleeding. Persistent bleeding beyond critical phase requires further investigations.[14,15,16]

In the absence of bleeding there is no role of either platelet transfusions or fresh frozen plasma and in some cases may they may increase the risk of pulmonary edema. Use of recombinant activated factor VII is not based on scientific evidence; rather it might be harmful in presence of an over activation of coagulation system. There is no role of Vitamin K, Tranexamic acid or IV immunoglobulins.[17,18,19]

Indications for respiratory support

Respiratory support is needed in cases of metabolic acidosis or when pCO_2 is higher than expected to compensate for acidosis.[20] In patients with encephalopathy and Glasgow coma scale of < 9, intubation is often required for airway protection.[21,22]

Indications for hemodynamic support

Appropriate fluid replacement should be the first step in hemodynamic support as vasopressors while being useful carry the risk of aggravating tissue hypoxia, they should be administrated only when there is marked hemodynamic instability (mean arterial pressure <60 mm of Hg).[23]

Use of Invasive procedures

Central venous catheter (CVC) insertion

Because of bleeding diathesis, peripheral vessels should be used. Moreover, in case of femoral, internal jugular or subclavian veins; it might be difficult to stop bleeding by to compression of the site. Risk of bleeding from venous access sites varies from 0-15.5 percent.[24]

CVC might be indicated in case peripheral venous approach is difficult, or inotropic support is required for blood pressure control. Similarly monitoring of central venous pressure may require a CVC insertion in critically ill patients especially after a surgical procedure. Preferably in such cases CVC should be inserted by ultrasound guidance.[25,26]

Out of multiple options subclavian is least appropriate as it is not accessible for compression.[27,28]

Arterial catheter insertion

Intra-arterial cannulation carries 1.8-2.6% risk of bleeding.[29]

Gastric tube

Usually not required but in case it is considered necessary use orogastric rather than nasogastric route as the former is less likely to cause bleeding.

Diagnostic/ Therapeutic drainage of pleural fluid

Pleural effusion drainage carries a small but significant risk of severe hemorrhage and sudden circulatory collapse. In case of respiratory distress, mechanical ventilation should be considered.[30]

Prevention of Dengue transmission in hospital

During febrile phase patients are infectious and guidelines advise use of mosquito netting and repellents to reduce nosocomial infection.[31]

Dengue fever in pregnancy

Generally, the presentation and the course is similar to non-pregnant patients[32,33] though diagnosis of certain complications like toxemia of pregnancy and HELLP syndrome may be difficult due to overlapping features.[34] Risk for in utero death and prematurity are increased in serious cases. Abruptio placenta is another important complication of Dengue fever during pregnancy.[33,35]

Diagnosis of plasma leakage in case of dengue fever may be difficult due to following physiological alterations in advanced pregnancy.

1. Elevation of HCT is masked by increased plasma volume in second and third trimester.
2. Clinical detection of ascites is difficult in the presence of gravid uterus.
3. Pulse pressure is high with a small fall in blood pressure.
4. A higher than normal resting pulse

As the risk for bleeding is highest during the critical phase (first 48 hours), induction of labor during this period should be avoided if possible. C-section is also hazardous during initial phase of illness. After the delivery, baby should be assessed for the possibility of transmission of disease.[34]

Dengue fever in immune-compromised patients

As a rule, clinical presentation is similar to immunocompetent patients. Diagnostic and therapeutic principles are the same with the difference that broad spectrum antibiotics should be started, after taking blood samples for culture/sensitivity; in case of serious neutropenia (neutrophil count <500/ml) and temperature > 38.3 C.[36]

Antihypertensive treatment in Dengue fever

Diuretics must be stopped. Patients taking diuretics for some other indication (like Heart failure) must be individually evaluated. A six-hourly monitoring of blood pressure is required and a progressive fall of blood pressure should be a warning sign of impending circulatory failure and an indication of stopping anti-hypertensive drugs which may be reintroduced one by one once the clinical condition is stable again.

Dengue fever in patients on antithrombotic therapy

Management of these patients is problematic with a risk of bleeding compounded by antithrombotic/anticoagulant drugs, while hemoconcentration and rising HCT can pose challenges. As a rule, need for anticoagulants/ antithrombotic can be considered for patients with a particular high risk of thrombosis.

Salicylates should be avoided except for those with a high risk of thrombosis/ embolism. thromboembolism

Following situations are considered high risk with an obligatory need of anti-coagulation therapy:

1. Angioplasty with stent insertion: in last one month for bare-metal and 3-6 months for drug-eluting stents
2. Mechanical valve especially mitral or tricuspid
3. Atrial fibrillation, multiple mechanical valves and history of thromboembolism.
4. Decreased ejection fraction (EF), old age, history

of stroke, mural thrombosis hypertension and diabetes mellitus.

In these patients, antiplatelet treatment may be continued. Withhold anticoagulant therapy if previously being given to patient. Heparin may be used with an aim to keep INR within acceptable therapeutic range. However anti-coagulants should be withheld if platelet are < 50,000/l, there are signs of overt bleeding, abnormal coagulation profile or circulatory shock.

Following categories should be considered low risk with use of anti-thrombotic/anti-coagulant as non-obligatory.

1. Stable coronary artery disease
2. Stent insertion more than six months before.
3. Atrial fibrillation with no other risk factor
4. Biological valve

In these patients withhold antiplatelet and anticoagulant therapy for one week.[37]

Discharge criteria

Before deciding to discharge the patient, medical team should ensure that patient.[4,12]

1. Is afebrile for at least two days
2. Is clinically stable
3. No anorexia/ vomiting and oral intake has started
4. HCT is stable for at least 24 hours
5. Platelets are at least > 40,000 with a rising trend
6. No respiratory distress due to pleural/ ascetic fluid
7. Minimal or no bleeding
8. Fully recovered organ dysfunction

REFERENCES

1. Rasheed SB, Butlin RK, Boots M. A review of dengue as an emerging disease in Pakistan. Public Health 2013; 127: 11-7.
2. Wichmann O, Hongsiriwon S, Bowonwatanuwong C, Chotivanich K, Sukthana Y, Pukrittayakamee S. Risk factors and clinical features associated with severe dengue infection in adults and children during the 2001 epidemic in Chonburi, Thailand. Trop Med Int Health. 2004; 9: 1022-9.
3. Wills BA, Oragui EE, Stephens AC, Daramola OA, Dung NM, Loan HT, et al. Coagulation abnormalities in dengue hemorrhagic fever: serial investigations in 167 Vietnamese children with dengue shock syndrome. Clin Infect Dis. 2002; 35: 277-85.
4. Kalayanarooj S, Nimmannitya S. Guidelines for DHF case management for workshop on case management of Dengue Hemorrhagic fever. WHO collaborating center for case management of Dengue/DHF/DSS. June 10-15, 2002.
5. Dung NM, Day NP, Tam DT, Loan HT, Chau HT, Minh LN, et al. Fluid replacement in dengue shock syndrome: a randomized double-blind comparison of four intravenous-fluid regiments. Clin infect Dis. 1999; 29: 787-94.
6. Nhan NT, Phuong CX, Kneen R, Wills B, Van My N, Phuong NT, et al. Acute management of dengue shock syndrome: a randomized double-blind comparison of 4 intravenous fluid regimens in the first hour. Clin Infect Dis. 2001; 32: 204-13.
7. Wills BA, Dung NM, Loan HT, Tam DT, Thuy TT, Minh LT, et al. Comparison of three fluid solutions for resuscitation in dengue shock syndrome. N Engl J Med. 2005; 353: 877-89.
8. Dengue hemorrhagic fever: diagnosis, treatment, prevention and control. 2nd ed. Geneva: World health organization: 1997. Available at http//w3.who.
9. Wills BA, Oragui EE, Stephens AC, Daramola OA, Dung NM, Loan HT, et al. Coagulation abnormalities in dengue hemorrhagic fever: serial investigations in 167 Vietnamese children with dengue shock syndrome. Clin Infect Dis. 2002; 35: 277-8.
10. Wills B, Van Ngoc T, Van NT, Thuy TT, Thuy TT, Dung NM, et al. Hemostatic changes in Vietnamese children with mild dengue correlate with the severity of vascular leakage rather than bleeding. Am J Trop Med Hyg. 2009; 81: 638-4.
11. Mairuhu AT, Mac Gillavry MR, Setiati TE, Soemantri A, Ten Cate H, Brandjes DP, et al. Is clinical outcome of denguevirus infections influenced by coagulation and fibrinolysis? A critical review of the evidence. Lancet Infect Dis. 2003; 3: 33-41.
12. Subcommittee of technical experts on clinical management of DF/DGF. Guidelines on clinical management of dengue/dengue hemorrhagic fever. Sri Lanka. 2005. Available at http//www.epid.gov.il.pdf/guidelines.
13. Lum LC, Goh AY, Chan PW, El-Amin AL, Lam S. Risk factors for hemorrhage in severe dengue infections.J Paediatr. 2002; 140: 629-31.
14. Chairulfatah A, Setiabudi D, Agoes R, Colebunders R. Thrombocytopenia and platelet transfusions in dengue hemorrhagic fever and dengue shock syndrome. Dengue Bulletin. 2003; 27: 138-43.
15. Lum LC, Abdel-Latif ME, Goh AY, Chan PW, Lam SK. Preventive transfusion in DSS-is it necessary? Pediatr. 2003; 143: 682-4.
16. Chiu YC, Wu KL, Kuo CH, Hu TH, Chou YP, Chuah SK, et al. Endoscopic findings and management of dengue patients with upper gastrointestinal bleeding Am J Top Med Hyg. 2005; 73: 41-4.

17. Chuansumrit A, Wangruangsatid S, Lektrakul Y, Chua MN, Capeding MR, Bech OM, et al. Dengue study group. Control of bleeding in children with DHF using recombinant activated factor VII: a randomized, doble-blind, placebo-controlled study. Blood Coagul Fibrinolysis. 2005; 16: 549-55.
18. Chuansumrit A, Tangnaraiatchakir K, Lektakul Y. The use of recombinant activated factor VII for controlling life threatening bleeding in DSS. Blood Coagul Fibrinolysis. 2004; 15: 335-42.
19. United Kingdom Hemophilia Center Doctors Organisation (UKHCDO) Guidelines on the selection and use of therapeutic products to treat hemophilia and oter hereditary bleeding disorders. Hemophilia. 2003; 9: 1-23.
20. Marino PL. Principles of mechanical ventilation. 3rd ed. USA: Lippincolt Williams and Wilkins. 2007; p: 461.
21. Riley B. Oh's intensive Care Manual. 5thed, China: Butterworth-Heinmann; Elsevier Limited. 2003: p: 496.
22. Pinnock CA, Lin T, Smith T. Indications for intubations and ventilatiolns after head injury. In Fundamentals of anesthesia. 2nd edition. Cambridge university press; 2002; P: 179.
23. Task force of the American college of clinical care medicine. Society of critical care medicine. Practice parameters for hemodynamic support of sepsis in adult patients in sepsis. Crit Care Med. 1999; 27: 639-60.
24. Graber D. Daile RH. Catheter flow rates updated. JACEP. 1977; 6: 518.
25. Doerfler ME, Kaufman B, Goldenberg AS. Central venous catheter placement in patients with disorders of hemostasis. Chest. 1996; 110: 185-88.
26. Mumtaz H, Williams V, Hauer-Jensen M, Rowe M, Henry-Tillman RS, Heaton KM, et al. Central venous catheter placement in patients with disorders of hemostasis. Am J surg. 2000; 180: 503-5.
27. McGee DC, Gould MK. Current concepts: preventing complications of central venous catheters. New Eng J Med. 2003; 348: 1123-33.
28. Taylor RW, Palagiri AV. Central venous catheterization. Crit Care Med. 2007; 35: 1390-6.
29. Frezza EE, Mezghebe H. Indications and complications of arterial catheter use in surgical or medical intensive care units: analysis of 4932 patients. Am Surg. 198; 64: 127-31.
30. Soni A, Chugh K, Sachdev A, Gupta D. Management of dengue fever in ICU. Indian J Pediatr. 2001; 68: 1051-5.
31. Wang WK, Chao DY, Kao CL, Wu HC, Liu YC, Li CM, et al. High levels of plasma dengue viral load during defervescence in patients with dengue hemorrhagic fever: Implications for pathogenesis. Virology. 2003; 305: 330-8.
32. Waduge R, Malavige GN, Pradeepan M, Wijeyaratne CN, Fernando S, Seneviratne SL. Dengue infections during pregnancy: a case series from Sri Lanka ad review of the literature, J Clin Virol. 2006; 37: 27-33.
33. Ismail NA, Kampan N, Mehdy ZA. Dengue in pregnancy. South Asia J Trop Med Public health. 2006; 37: 681-3.
34. De Roeck D, Deen J, Clemens JD. Policymakers views on dengue fever/dengue hemorrhagic fever and the need for dengue vaccination in four south Asian countries. Vaccine. 2003; 22: 121-9.
35. Carles G, Peiffer H, Talarmin A. Effects of dengue fever during pregnancy in French Guiana. Clin Infect Dis. 1999; 28: 637-40.
36. Darrigo LG, Carvlaho AM, Martins C. Chikungunya, Dengue and Zika in immunocompromised hosts. Curr infect Dis Rep. 2018; 20: 5.
37. Verdeal JC, Costa Filho R, Vanzillotta C, Macedo GL, Bozza FA, Toscano L, et al. Rev Bras Ter Intensiva. 2011; 23: 125-33.