**Original Research Article**

**International Journal of Medical and Health Research**
**ISSN: 2454-9142**
**Received: 19-09-2019; Accepted: 23-10-2019**
**www.medicalsciencejournal.com**
**Volume 5; Issue 11; November 2019; Page No. 104-108**

# Clinical assessment of dengue fever with respect to hematological profile in pediatric cases of north-Bihar region

**Dr. K N Mishra[1], Dr. Sanjay Kumar Nirala[2*]**

[1] Professor & HOD, India Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India
[2] Junior Resident, Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India
[*] Corresponding Author: Dr. Sanjay Kumar Nirala

**Abstract**
Dengue is one of the most important viral diseases especially in the tropical regions. According to the WHO almost 50 million people get dengue infection annually and WHO estimates almost half of the world's population lives in countries having endemicity for dengue infection. Most common clinical presentation of Dengue fever (DF) is of an acute febrile viral disease with headaches, bone, joint and muscular pains, rash and leucopenia. It is also known as break bone fever due to the severe bone pains. Dengue hemorrhagic fever (DHF) is characterized by four major clinical manifestations: high grade fever, hemorrhagic phenomena, often with hepatomegaly and, in severe cases, signs of circulatory failure. Severe plasma leakage in these patients can lead to hypovolemic shock and circulatory failure. This is called dengue shock syndrome (DSS) and can lead to death. Hence based on above findings the present study was planned to evaluate the Clinical Assessment of Dengue Fever with Respect to Haematological Profile in Pediatric Cases from Bihar Region.
The present study has been done in Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India. Total 30 cases of the dengue were enrolled in the present study. All the routine investigations like complete blood count (haematology auto-analyser, sysmax xs800i), peripheral blood film for cell morphology, thick and thin blood smear for malaria parasite, specific malarial antigen card test, random blood sugar, complete urine examination, were done. Dengue IgM and IgG by ELISA was done in all the cases. In a few cases chest X-ray PA view, liver function tests, renal function tests and ultrasonography of abdomen were also done.
From the present study it can be concluded that dengue fever is a viral infection caused by transmission of the virus through mosquitoes, and accurate physical examination and proper follow-up of haematological changes are needed to decrease morbidity and mortality among children.

**Keywords:** dengue, fever, haematological profile, etc

## Introduction
Dengue is fast emerging pandemic-prone viral disease in many parts of the world. Dengue flourishes in urban poor areas, suburbs and the countryside but also affects more affluent neighbourhoods in tropical and subtropical countries. Dengue is a mosquito-borne viral infection causing a severe flu-like illness and, sometimes causing a potentially lethal complication called severe dengue. The incidence of dengue has increased 30-fold over the last 50 years. Up to 50-100 million infections are now estimated to occur annually in over 100 endemic countries, putting almost half of the world's population at risk. Severe dengue (previously known as dengue haemorrhagic fever) was first recognized in the 1950s during dengue epidemics in the Philippines and Thailand. Today it affects Asian and Latin American countries and has become a leading cause of hospitalization and death among children and adults in these regions.
The full life cycle of dengue fever virus involves the role of mosquito as a transmitter (or vector) and humans as the main victim and source of infection. The dengue virus (DEN) comprises four distinct serotypes (DEN-1, DEN-2, DEN-3 and DEN-4) which belong to the genus Flavivirus, family Flaviviridae. Distinct genotypes have been identified within each serotype, highlighting the extensive genetic variability of the dengue serotypes. Among them, "Asian" genotypes of DEN-2 and DEN-3 are frequently associated with severe disease accompanying secondary dengue infections. The Aedes aegypti mosquito is the main vector that transmits the viruses that cause dengue. The viruses are passed on to humans through the bites of an infective female Aedes mosquito, which mainly acquires the virus while feeding on the blood of an infected person. Once infected, humans become the main carriers and multipliers of the virus, serving as a source of the virus for uninfected mosquitoes. The virus circulates in the blood of an infected person for 2-7 days, at approximately the same time that the person develops a fever. Patients who are already infected with the dengue virus can transmit the infection via Aedes mosquitoes after the first symptoms appear (during 4-5 days; maximum 12).
Dengue is the most common and important arthropod-borne viral (arboviral) illness in humans. It is transmitted by mosquitoes of the genus Aedes, which are widely distributed in subtropical and tropical areas of the world (see the image below). The incidence of dengue has increased dramatically in recent decades, with estimates of 40%-50% of the world's population at risk for the disease in tropical,

subtropical, and, most recently, more temperate areas [1].

A small percentage of persons who have previously been infected by one dengue serotype develop bleeding and endothelial leak upon infection with another dengue serotype. This syndrome is termed severe dengue (also known as dengue haemorrhagic fever and dengue shock syndrome). Dengue fever is typically a self-limited disease with a mortality rate of less than 1% when detected early and with access to proper medical care. When treated, severe dengue has a mortality rate of 2%-5%, but, when left untreated, the mortality rate is as high as 20%.

The initial phase of severe dengue is similar to that of dengue fever and other febrile viral illnesses. Shortly after the fever breaks (3-7 days after symptom onset or sometimes within 24 hours before), signs of plasma leakage appear, along with the development of hemorrhagic symptoms such as bleeding from sites of trauma, gastrointestinal bleeding, and hematuria. Patients may also present with severe abdominal pain, persistent vomiting that may contain blood, fatigue, and febrile seizures (in children).

The subsequent 24 hours frequently prove critical. If left untreated, hemorrhagic fever most likely progresses to shock. Common symptoms in impending shock include abdominal pain, vomiting, and restlessness. Patients also may have symptoms related to circulatory failure, such as pallor, tachypnea, tachycardia, dizziness/light headedness, and a decreased level of consciousness.

Dengue is the most common and important arthropod-borne viral (arboviral) illness in humans. Globally, 2.5-3 billion individuals live in approximately 112 countries that experience dengue transmission. While the annual incidence is unclear owing to incomplete global reporting and misclassification of illness, approximately 3.2 million individuals were infected globally in 2015. It is caused by infection with 1 of the 4 serotypes of dengue virus, which is a Flavivirus (a genus of single-stranded non-segmented RNA viruses). Infection with one dengue serotype confers lifelong homotypic immunity to that serotype and a brief period (approximately 2 years) of partial heterotypic immunity to other serotypes, but an individual can eventually be infected by all 4 serotypes. Several serotypes can be in circulation during an epidemic.

Dengue is transmitted by mosquitoes of the genus Aedes, which are widely distributed in subtropical and tropical areas of the world (see the image below). An individual with dengue is capable of transmitting the virus for 4-5 days (maximum, 12 days) to a capable vector. After an incubation period of 5-10 days, the infected mosquito can transmit virus for the rest of its life span (2 weeks to 1 month). Aedes albopictus is more cold tolerant than Aedes aegypti, so it can survive and transmit virus in the more temperate regions of the United States and Europe.

The global incidence of dengue has increased dramatically in the last several decades, with an estimated 40%-50% of the world's population in 128 countries at risk [2, 3, 4]. Today, severe dengue largely affects Asian and Latin American countries, where it is a leading cause of hospitalization and death. The World Health Organization (WHO) ranked dengue as one of the top ten threats to global health in 2019. [5]

Initial dengue infection may be asymptomatic (50%-90%), [6] may result in a nonspecific febrile illness, or may produce the symptom complex of classic dengue fever (DF). Classic dengue fever is marked by rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation, and a centrifugal maculopapular rash, among other manifestations. The severity of the pain led to the term breakbone fever to describe dengue. A small percentage of persons who have previously been infected by one dengue serotype develop bleeding and endothelial leak upon infection with another dengue serotype. This syndrome is termed severe dengue (reclassified in 2009 by the WHO, previously referred to as dengue hemorrhagic fever and dengue shock syndrome).

Severe dengue has also been termed dengue vasculopathy. Vascular leakage in these patients results in hemoconcentration and serous effusions and can lead to circulatory collapse. This, in conjunction with severe hemorrhagic complications, can lead to a shock syndrome, which poses a greater fatality risk than bleeding per se [7].

Dengue virus transmission follows 2 general patterns: epidemic dengue and hyperendemic dengue. Epidemic dengue transmission occurs when dengue virus is introduced into a region as an isolated event that involves a single viral strain. If the number of vectors and susceptible pediatric and adult hosts is sufficient, explosive transmission can occur, with an infection incidence of 25-50%. Mosquito-control efforts, changes in weather, and herd immunity contribute to the control of these epidemics. Transmission appears to begin in urban centers and then spreads to the rest of the country [8]. This is the current pattern of transmission in parts of Africa and South America, areas of Asia where the virus has reemerged, and small island nations. Travelers to these areas are at increased risk of acquiring dengue during these periods of epidemic transmission.

Hyperendemic dengue transmission is characterized by the continuous circulation of multiple viral serotypes in an area where a large pool of susceptible hosts and a competent vector (with or without seasonal variation) are constantly present. This is the predominant pattern of global transmission. In areas of hyperendemic dengue, antibody prevalence increases with age, and most adults are immune. Hyperendemic transmission appears to be a major risk for dengue hemorrhagic fever. Travelers to these areas are more likely to be infected than are travelers to areas that experience only epidemic transmission [9].

Because the signs and symptoms of dengue fever are nonspecific, attempting laboratory confirmation of dengue infection by serodiagnosis, reverse-transcriptase polymerase chain reaction (RT-PCR), or culture is important. Serodiagnosis is made on the basis of a rise in antibody titer in paired IgG or IgM specimens. Results vary depending on whether the infection is primary or secondary (see Presentation and Workup). Dengue is a reportable disease in the United States; known or suspected cases should be reported to public health authorities. Dengue fever is usually a self-limited illness. Supportive care with analgesics, judicious fluid replacement, and bed rest is usually sufficient. Successful management of severe dengue requires intravascular volume replacement, with careful attention to fluid management and proactive treatment of hemorrhage. Admission to an intensive care unit is indicated

for patients with severe dengue.

In humans recovery from infection by one dengue virus provides lifelong immunity against that particular virus serotype. However, this immunity confers only partial and transient protection against subsequent infection by the other three serotypes of the virus. Evidence points to the fact that sequential infection increases the risk of developing severe dengue. The time interval between infections and the particular viral sequence of infections may also be of importance.

Dengue is one of the most important viral diseases especially in the tropical regions. According to the WHO almost 50 million people get dengue infection annually and WHO estimates almost half of the world's population lives in countries having endemicity for dengue infection [10]. Most common clinical presentation of Dengue fever (DF) is of an acute febrile viral disease with headaches, bone, joint and muscular pains, rash and leucopenia. It is also known as break bone fever due to the severe bone pains [11]. Dengue hemorrhagic fever (DHF) is characterized by four major clinical manifestations: high grade fever, hemorrhagic phenomena, often with hepatomegaly and, in severe cases, signs of circulatory failure. Severe plasma leakage in these patients can lead to hypovolemic shock and circulatory failure. This is called dengue shock syndrome (DSS) and can lead to deat [12]. Hence based on above findings the present study was have been done to evaluate the Clinical Assessment of Dengue Fever with Respect to Haematological Profile in Pediatric Cases of north- Bihar Region.

## Methodology

The present study has been done in Department of Pediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India. Total 30 cases of the dengue were enrolled in the present study. All the routine investigations like complete blood count (haematology auto-analyser, sysmax xs800i), peripheral blood film for cell morphology, thick and thin blood smear for malaria parasite, specific malarial antigen card test, random blood sugar, complete urine examination, were done. Dengue IgM and IgG by ELISA was done in all the cases. In a few cases chest X-ray PA view, liver function tests, renal function tests and ultrasonography of abdomen were also done.

For routine investigations venous blood was collected from cubital vein from all patients admitted with symptoms suggestive of dengue fever. Evaluation of haematological parameters was done by collecting 2 ml samples in EDTA containers which were examined for Haemoglobin count, Haematocrit, Platelet count, Total leucocyte count, Differential leucocyte count. The analysis was done by the automated analyser SYSMEX XT 1800i (3-part differential).

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: Childrens with serologically confirmed IgM positive dengue fever with or without purpuric rash admitted to Medicine ward. Childrens of both genders.

Exclusion criteria: Pre-existing chronic diseases. Childrens who were having mixed infections like Dengue fever and Malaria and where diagnosis was not confirmed were excluded from the study. Children proved to have malaria, cancer, tuberculosis, HIV, and bacterial and parasitic illnesses, and those who were on any medications (antibiotics, antipyretics, anti-inflammatory) for the past 2 months.

## Results and Discussion

There are many risk factors that help spread of this virus such as travelling of some persons from endemic areas such as India, Pakistan, Yemen, and other tropical or subtropical regions, and also rain falling, increased humidity, and presence of water collection sites which help breeding of mosquitoes. Early diagnosis based on laboratory investigations and management of DF is mandatory, and it should be a priority for not only patients but also for the entire public health. Diagnosis of dengue virus infection based on clinical symptoms and signs is not reliable and should be confirmed by laboratory studies [13].

Clinical spectrum of Dengue virus infection can be into asymptomatic, Dengue fever with or without accompanying bleeding, dengue hemorrhagic with or without shock and expansion syndrome Dengue manifestation [14, 16, 18]. Various signs occur both the result of clinical and laboratory depend on the pathogenesis of the patient. In infants primarily, the symptoms of Dengue infection tend to experience progression towards severe symptoms more rapidly than children and adults. It is due to several reasons such as infant's hemodynamic ability not yet competent enough to compensate for the state of the plasma leak syndrome during Dengue infection and the Antibody-Dependent Enhancement (ADE) mechanism that occurs when the infant is infected. The second Dengue virus with a different serotype than the first infected times on her or her mother. In infants, there may also be a vertical transmission of the virus from mother to child through the placenta [15, 17].

**Table 1:** Demographic details

| Demographic data | No. of Cases |
|---|---|
| Total Cases enrolled | 30 |
| Males | 18 |
| Females | 12 |
| Age (years) | 4 – 12 years |
| Average days of hospitalization | 3 – 7 days |
| Death | 0 |
| Discharge | 30 |

**Table 2:** Distribution of dengue cases as per revised WHO criteria

| Classification | Number of cases |
|---|---|
| Dengue without warning signs | 6 |
| Dengue with warning signs | 22 |
| Severe dengue | 2 |
| Total | 30 |

**Table 3:** Clinical manifestation according to type of dengue fever cases.

| Symptoms and sign | Number of cases |
|---|---|
| Fever | 27 |
| Myalgia | 27 |
| Headache | 16 |
| Cough | 4 |
| Abdominal pain | 3 |
| Rashes | 2 |
| Epistaxis | 1 |
| Hepatosplenomegaly | 2 |
| Gum bleeding | 1 |
| Hematuria | 1 |
| Vomiting | 12 |
| Retro-orbital pain | 5 |

**Table 4:** Laboratory parameters in dengue fever cases.

| Criteria | No. of cases |
|---|---|
| Raised hematocrit >35% | 15 |
| Leucopenia <5000 | 13 |
| Thrombocytopenia <1.5 lakh/cu mm | 25 |
| Thrombocytopenia <1 lakh/cu mm | 18 |
| Thrombocytopenia <50000/cu mm | 4 |
| Serum bilirubin>2 mg/dl | 5 |
| Serum creatinine >1.5 mg/dl | 2 |

Mishra *et al.* [19] in their study observed that the mean age of hospitalized patients was 8.7 years. 63.9% of patients were admitted in the hospital for 3–6 days. Seven children out of 13 severe dengue patients were admitted for more than 6 days. The mean tenure of hospitalization was 3.8 days. Mishra *et al.* [19] also observed fever in 100% of the cases, myalgia in 76.8% and abdominal pain in 54.3% cases. The most common bleeding manifestations in both severe and non-severe dengue were petechiae seen in 22.1% cases.

In the study by Srinivasa *et al.* [20] the most common affected age group was that of school going children (42%) and adolescents (36%). Srinivasa *et al.* [10] studied 200 cases and observed that all the cases all had fever (100%), 144 (72%) had vomiting, 92(46%) had abdominal pain, 67(33.5%) had hepatomegaly, 21 (10.5%) had rashes, 4(2%) had splenomegaly, 26(13%) had bradycardia and 47(23.5%) developed hypotension and shock. The most common bleeding manifestation was petechiae (6.2%) followed by hemetemes is in 4.1% and epistaxis in 3.6% cases.

In the study by Jain *et al.* [21] the most common age group was between 5 to 10 years (46%) followed by 1-5 year age group. Infants were only 7.6% and the youngest one was 7 months old. Our findings compare well with the above observations. Jain *et al.* [21] observed fever in all dengue patients with mean duration of 5.6 days. The common presentation by these children included headache (64%), myalgia (63%), bleeding (58%) and decreased urine output (53%). Among the clinical findings, hepatomegaly and splenomegaly were noted in 90% and 26% of the cases respectively. Clinical fluid accumulation in form of ascites and pleural effusion with reduced air entry were observed in 40% and 43% of cases.

In the study by Kumar *et al.* [22] majority 175 (57%) were in the age group of 6–12 years, 84 (27%) in the age group of 1–5 years, and 47 (16%) were infants. The mean age of the study population was estimated to be 7.8±3.2 years. Kumar *et al.* [22] observed fever in all of their patients, with the duration of hospital stay <5 days in 205 (72%) and 5–10 days in 75 patients (25%). The most common symptoms were vomiting in 168 (54.90%), abdominal pain in 111 (36.3%), bleeding manifestation in 43(14.05%), headache in 41(13.40%), myalgia in 32 (10.5%), and lethargy (9.8%). The other symptoms observed in their study were arthralgia (9.5%), altered sensorium (7.8%), rash (7.2%), diarrhea (6.5%), oliguria (6.5%), cough/rhinitis (5.2%), anorexia (3.9%), and retro-orbital pain (1.3%).

In the study by Alam *et al.* [23] the age ranged from 6 months to 15 years with a mean of 6.5± 3.5 years and about half (51.9%) of them were between 5-10 years age. Alam *et al.* [23] observed fever >5 days duration in 63% children with continued type of fever being predominant (75.9%). About 60% of patients had abdominal pain, 57% vomiting, 46.3% myalgia, 31.5% had headache, 18.5% arthralgia, 14.8% retro-orbital pain, 9.3% loose stool and 3.7% had runny nose/cough.

In various studies thrombocytopenia, bleeding episodes and neurological complications were found to have a significant association with severity of dengue [24, 25]. Hepatomegaly was found to have a significant association with severity in a study by Sahana *et al.* 13 Splenomegaly was seen more in non survivors than survivors in a study by Reddy BK *et al.* [26] Many studies proposed hemo-concentration as a prognostic factor for the severity of dengue infection [26, 27]. Vasculopathy in dengue causes increased vascular permeability, leading to hemo-concentration and shock. A falling trend in platelet count as seen by Jayashree K *et al.* and Mourao *et al.* was associated with poor outcome [28, 29]. The platelets fall before the patient enters into a state of shock. Low platelets are explained by bone marrow suppression and immune response induced platelet destruction by the liver and spleen [30].

## Conclusion

From the present study it can be concluded that dengue fever is a viral infection caused by transmission of the virus through mosquitoes, and accurate physical examination and proper follow-up of haematological changes are needed to decrease morbidity and mortality among children.

## References


1. World Health Organization. Dengue and severe dengue fact sheet. WHO. Available at http://www.who. int/mediacentre/factsheets/fs117/en/. April 2017; Accessed: September 28, 2017.
2. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL. *et al.* The global distribution and burden of dengue. Nature. 2013; 496(7446):504-7.
3. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG. *et al.* Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis. 2012; 6(8):e1760.
4. Wilson ME, Chen LH. Dengue: update on epidemiology. Curr Infect Dis Rep. 2015; 17(1):457.
5. Ten threats to global health in 2019. World Health Organization. Available at https://www.who.int/emergencies/ten-threats-to-global-health-in-2019. 2019; Accessed: Feb 2, 2019.
6. Kyle JL, Harris E. Global spread and persistence of dengue. Annu Rev Microbiol. 2008; 62:71-92.
7. Statler J, Mammen M, Lyons A, Sun W. Sonographic findings of healthy volunteers infected with dengue

virus. J Clin Ultrasound. 2008; 36(7):413-7.
8. Gubler DJ. Cities spawn epidemic dengue viruses. Nat Med. 2004; 10(2):129-30.
9. Wilder-Smith A, Gubler DJ. Geographic expansion of dengue: the impact of international travel. Med Clin North Am. 2008; 92(6):1377-90, x.
10. World Health Organisation. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control, New Edition, World Health Organization and TDR for research on diseases of poverty, 2009.
11. Hales S, De Wet N, Maindonald J, Woodward A. Potential effect of population and climate changes on global distribution of dengue fever: an empirical model. The Lancet. 2002; 360(9336):830-34.
12. Siqueira JB, Martelli SMT, Coelho GE, Simplício ACR, Hatch DL. Dengue and dengue hemorrhagic fever, Brazil, 1981–2002. Emerging infectious diseases. 2005; 11(1):48-53.
13. Seok MW, Shamala DS. Evaluation of a commercial SD dengue virus NS1 antigen capture enzyme-linked immunosorbent assay kit for early diagnosis of dengue virus infection. J Clin Microbiol. 2010; 48:2793-2797.
14. World Health Organization 2009 Dengue guideline for diagnosis, treatment, prevention and control (Geneva Switzerland: World Health Organization Press)
15. Jain A, Chaturvedi U. Dengue in infants: an overview Fems. Immunol. Med. Microbiol. 2010; 59(2)119-30
16. World Health Organization Comprehensive guideline for prevention and control for dengue and dengue hemorrhagic fever (New Delhi India: Regional Office for South-East Asia), 2011.
17. Elling R, Henneke P, Hatz C, Hufnagel M. Dengue fever in children: where are we now? Pediatr. Infect. Dis. J. 2013; 32(9):1020.
18. Dorland's Illustrated Medical Dictionary 32nd edition (Philadelphia: Elsevier Health Sciences) p486.
19. Mishra S, Ramanathan R, Agarwalla SK. Clinical Profile of Dengue Fever in Children: A Study from Southern Odisha, India. Scientifica, 2016. Article ID 6391594, 6 pages.
20. Srinivasa S, Nawab T, Nair CC. Clinical profile and ultrasonographic findings in children with dengue fever. Curr Pediatr Res. 2014; 18(2):87-90.
21. Jain H. Clinical profile and outcome of dengue fever in hospitalized children of South Rajasthan, India. Int J Contemp Pediatr. 2016; 3(2):546-549.
22. Kumar BV, Simna L, Kalpana D, Kailas L. Clinical profile and outcome of children admitted with dengue fever in a tertiary care hospital in South India. Indian J Child Health. 2018; 5(1):32.
23. Alam AS, Sadat SA, Swapan Z, Ahmed AU, Karim MdK, Paul HK, *et al.* Clinical profile of dengue fever in children. Bangladesh J Child Health. 2009; 33(2):55-58.
24. Gupta V, Yadav TP, Pandey RM, Singh A, Gupta M, Kanaujiya P. *et al.* Risk factors of dengue shock syndrome in children. J Trop Pediatr. 2011; 57(6):451-6.
25. Hendarto SK, Hadinegoro SR. Dengue encephalopathy. Acta Paediatr Jpn. 1992; 34(3):350-7.
26. Chacko B, Subramanian G. Clinical, laboratory and radiological parameters in children with dengue fever and predictive factors for dengue shock syndrome. J Trop Pediatr. 2008; 54(2):137-40.
27. Shah GS, Islam S, Das BK. Clinical and laboratory profile of dengue infection in children. Kathmandu Univ Med J (KUMJ). 2006; 4(1):40-3.
28. Jayashree K, Manasa GC, Pallavi P, Manjunath GV. Evaluation of platelets as predictive parameters in dengue fever. Indian J Hematol Blood Transfus. 2011; 27(3):127-30.
29. Mourao MP, Lacerda MV, Macedo VO, Santo JB. Thrombocytopenia in patients with dengue virus infection in Brazilian Amazon. Platelets. 2007; 18(8):605-12.
30. Chuansumrit A, Tangnararatchakit K. Pathophysiology and management of dengue hemorrhagic fever. Transfus Altern Transfus Med. 2006; 8(1):S3-11.