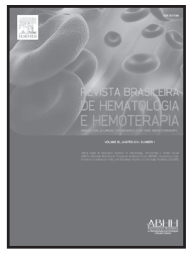
Revista Brasileira de Hematologia e Hemoterapia
Brazilian Journal of Hematology and Hemotherapy
www.rbhh.org



Original article

# Clinical and laboratory characteristics of patients with dengue hemorrhagic fever manifestations and their transfusion profile

*Denys Eiti Fujimoto*[a,*], *Sergio Koifman*[b]

[a] *Universidade Federal do Acre (UFAC), Rio Branco, AC, Brazil*
[b] *Fundação Oswaldo Cruz (Fiocruz), Rio de Janeiro, RJ, Brazil*

ARTICLE INFO

*Article history:*
Received 6 July 2013
Accepted 18 December 2013

*Keywords:*
Dengue hemorrhagic fever
Blood transfusion
Hemorrhagic disorders
Platelet transfusion

ABSTRACT

*Background:* Dengue is an infectious disease with a recurring incidence, especially in developing countries. Despite recent economic growth, success in disease control has not been achieved, and dengue has evolved from cyclic epidemic outbreaks to a lack of seasonality. The lack of scientific basis for the proper management of cases with hemorrhagic manifestations, especially regarding transfusion procedures, might contribute to the high death rate in potentially avoidable cases.
*Objective:* The aim of the study was to identify the clinical and laboratory manifestations in hemorrhagic dengue fever treated at the emergency services in Rio Branco, AC, Brazil, as well as to describe transfusion characteristics of patients and identify possible prognostic factors.
*Methods:* A retrospective descriptive study was performed to analyze the distribution of relative frequencies of clinical and laboratory variables. The study was carried out in Rio Branco with confirmed dengue fever cases. Secondary data were obtained by Acre Epidemiological Surveillance teams of cases with bleeding or platelet counts under $100.0 \times 10^9$/L. The patients' clinical, laboratory and transfusion data were obtained from hospital records.
*Results:* A total of 90,553 dengue cases were reported of which 7,447 had serologic confirmation; 267 cases had hemorrhagic manifestations and 193 patients were located. Nearly half of the patients had anemia and the mean of the lowest platelet count of these patients was $26.4 \times 10^9$/L. Platelet concentrate was transfused in 22.3% of cases with a mean of 7.5 IU/patient, fresh frozen plasma in 21.2% with a mean of 5.2 IU/patient and just 2.6% of patients received concentrated red blood cells with a mean of 3.2 IU/patient. Bleeding led to transfusions. Signs of plasma leakage and cardiopulmonary dysfunction were correlated to unfavorable outcomes.
*Conclusion:* The pattern of clinical and laboratory criteria observed in this investigation does not differ from the literature. Transfusions were used as part of the treatment of dengue hemorrhagic fever manifestations. Some of the clinical manifestations may be related to unfavorable outcomes.



*Corresponding author at:* Universidade Federal do Acre, Pró-Reitoria de Pós-Graduação, Programa de Pós-Graduação em Saúde Coletiva, BR 364, Km 04, Distrito Industrial, 69915-900, Rio Branco, AC, Brazil.
E-mail address: denys.fujimoto@hotmail.com (D.E. Fujimoto).
1516-8484/$ - see front matter © 2014 Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular. Published by Elsevier Editora Ltda. All rights reserved.
DOI: 10.5581/1516-8484.20140027

## Introduction

Dengue virus belongs to the genus Flavivirus (group B arbovirus, RNA virus) and comprises structural and non-structural proteins.[1] The classic clinical presentation is characterized by the abrupt onset of headache, myalgia and high fever, in addition to arthralgia, retro-orbital pain and hemorrhagic manifestations. The classical presentation differs from dengue hemorrhagic fever, which is characterized by fluid leakage into the interstitium.[2] Halstead states that in Latin American countries including Brazil, mosquito eradication was achieved in large urban centers after World War II, however, almost 20 years after, there was a resurgence of *Aedes* populations in Brazil. This allowed the first dengue outbreak with viral isolation in 1981 in Boa Vista, state of Roraima, along with the identification of DEN-1 virus and later of DEN-4 virus in 2007.[3] DEN-1 and DEN-2 were found in Rio de Janeiro in 1987 and DEN-3 in 2002. Between 2000 and 2005, Brazilian cases represented more than 60% of those registered by the World Health Organization (WHO) and almost 80% of all cases in the Americas.[4] This increase was identified in reports from the Brazilian Communicable Disease Information System.[5]

A quick dengue infection confirmation test is not available, and a complete blood count (CBC) might show characteristics such as leukopenia and thrombocytopenia.[6] These findings can be explained by peripheral platelet destruction mechanisms in the liver and spleen via the action of immunocomplexes or the complement system, in addition to the inhibition of medullary hematopoiesis[7] and disseminated intravascular coagulation.[8] A coagulogram might also indicate changes such as prolonged prothrombin and activated partial thromboplastin times, in addition to decreased serum fibrinogen concentration without increased levels of fibrinogen degradation products; these signs occur mainly with the hemorrhagic form of dengue fever.[9] According to Lupi, "[...] Increased aspartate aminotransferase (AST) can be observed in 30%-90% of classic dengue cases";[8] this increase might correlate with thrombocytopenia, and thus, the Sri Lanka Medical Association considers a normal AST level to be a strong negative predictor of dengue hemorrhagic fever and its complications.[10]

The Ministry of Health recommends platelet transfusion when platelet levels are less than $20 \times 10^9$/L with significant bleeding or when platelet counts range from 20-50 $\times 10^9$/L with suspected central nervous system (CNS) bleeding.[2] Singhi et al. recommends platelet concentrate transfusions at lower platelet counts (10 x $10^9$/L).[1] The authors of a population-based study conducted in India mentioned that 42.6% of the patients with confirmed dengue and thrombocytopenia (platelet count < $40 \times 10^9$/L) received platelet concentrate transfusions.[11] In Singapore, platelet transfusion was performed in approximately 12% (249 patients) of 1,973 cases with a mean platelet count of $15 \times 10^9$/L.[12]

The infusion of fresh frozen plasma (FFP) at a dose of 10 mL/kg given every 8 or 12 hours according to changes in the coagulogram, is also recommended.[2] However, a prospective, randomized, double-blind study was conducted to evaluate the efficacy of FFP versus isotonic saline solution infusions, and a significant increase in the platelet count was observed during the first 12 hours after infusion only in the FFP receiving group.[1]

The municipality of Rio Branco, located in the western Amazon region, has shown a marked annual increase in the incidence of dengue infections, especially since 2009,[5] and also an increase in the incidence of dengue hemorrhagic fever. Patients rely on emergency and urgent care services in two emergency healthcare units. The most serious cases and those that require transfusion are transferred to the Hospital de Urgência e Emergência de Rio Branco (HUERB).

Platelet concentrate and FFP transfusions have been used as a measure to prevent the increasing clinical evolution of dengue hemorrhagic fever, thus preventing evolution of the disease towards death. Nevertheless, the criteria for making a decision regarding the implementation of transfusion are not clearly defined, and therefore such decisions are made relatively empirically, based on the experience of emergency center health professionals.

## Objective

This study sought to determine the clinical and laboratory characteristics, transfusion aspects and mortality of patients with dengue hemorrhagic fever treated by emergency services in the city of Rio Branco, Acre.

## Methods

This retrospective descriptive study employed secondary data on dengue cases confirmed via serology by the State Epidemiological Surveillance Service. Only cases with bleeding or platelet counts less than $100 \times 10^9$/L from January 3rd, 2007 to June 14th, 2011 were included. Additional information was obtained from the medical records of the health services. Anemia was defined as hemoglobin levels less than 13.0 g/dL or hematocrit less than 40% for males, and a hemoglobin level less than 11.5 g/dL or hematocrit less than 36% for females at any point during hospitalization. Eosinophilia was defined as an eosinophil count above the normal range (0.04-0.4 $\times 10^9$/L) at any point during hospitalization. This project was approved by the Research Ethics Committee of the Universidade Federal do Acre (UFAC; number 23107.011739/2011-15). A relative frequencies analysis of clinical and laboratory variables and transfusion aspects was performed, and the distribution of parameters was determined with 95% confidence intervals. Additionally, the possible effect on mortality was compared between groups that did or did not receive platelet concentrate or FFP transfusions, according to the chi-squared method with the level of significance being set at 5%.

## Results

A total of 90,553 dengue cases were reported in Rio Branco during the study period. Serology was performed in

16.5% (14,985 cases) cases, 7,447 serologically confirmed (49.7%; Figure 1). Among the confirmed cases, 7,144 (99.6%) were classified as classic dengue, whereas 267 cases with hemorrhagic manifestations were identified as hemorrhagic dengue according to criteria set by this study. A subsequent survey identified the location of 193 of the latter cases (72.3%) in the medical records. A predominance of female patients was observed (57.0% of the hemorrhagic manifestation cases). The mean and median patient ages were 38.2 and 35 years, respectively (95% confidence interval [95% CI]: 35.3-41.2 years).

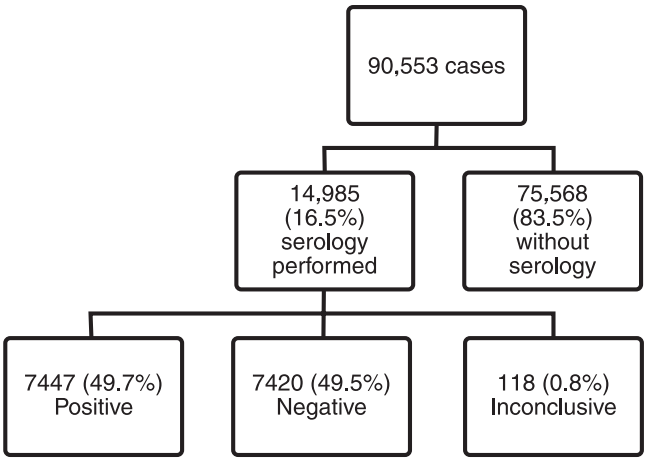



**Figure 1 – Hierarchical scheme of the first analysis of dengue cases in the city of Rio Branco, in the period 2007-2011.**

Table 1 shows the frequency distributions of the clinical characteristics at diagnosis and the pattern of clinical evolution observed in this study. Of the 193 medical records, 29 patients (15.0%; 95% CI: 10.3-20.9) reported some type of comorbidity. The most frequently reported comorbidity, in 41.4% (95% CI: 23.5-61.1) of the reports, was hypertension.

**Table 1 - Clinical characteristics in patients with dengue hemorrhagic fever admitted to emergency care services in Rio Branco, Acre from January 2007 to May 2011.**

| Signs and symptoms | n | % | 95% CI |
|---|---|---|---|
| Fever | 154 | 79.8 | 73.4-85.2 |
| Headache | 112 | 58.0 | 50.7-65.1 |
| Myalgia | 108 | 56.0 | 48.7-63.1 |
| Abdominal pain | 79 | 40.9 | 33.9-48.2 |
| Arthralgia | 68 | 35.2 | 28.5-42.4 |
| Vomiting | 56 | 29.0 | 22.7-36.0 |
| Retro-orbital pain | 31 | 16.1 | 11.2-22.0 |
| Skin rash | 27 | 14.0 | 9.4-19.7 |
| Lethargy | 21 | 10.9 | 6.9-16.2 |
| Itching | 17 | 8.8 | 5.2-13.7 |
| Respiratory distress | 12 | 6.2 | 3.3-10.6 |
| Painful hepatomegaly | 2 | 1.0 | 0.1-3.7 |

95% CI: 95% confidence interval.

The most frequently reported signs and symptoms, listed in order of incidence, were fever, headache and myalgia (Table 1). Bleeding occurred in 35.8% of the cases (95% CI: 29.0-43.0) and was mainly distributed as petechiae (14.0%), gingival bleeding (13.0%) and epistaxis (10.9%).

Plasma leakage was observed in 10.4% of the cases (95% CI: 6.4-15.6) and hypotension and hemodynamic instability occurred in 65.0% and 20.0% of these cases, respectively.

Fourteen cases (7.3%) evolved to death and 15 cases (7.8%) required intensive care. Among the observed complications, cardiorespiratory dysfunction was the most common affecting 5.7% of the cases, followed by ascites (4.7%) and pleural effusion (3.6%; Table 2).

**Table 2 - Clinical complications of patients with dengue hemorrhagic fever admitted to the emergency care services in Rio Branco, Acre from January 2007 to May 2011.**

| | n | % | 95% CI |
|---|---|---|---|
| *Complications* | | | |
| Cardiorespiratory dysfunction | 11 | 5.7 | 2.9-10.0 |
| Ascites | 9 | 4.7 | 2.2-8.7 |
| Pleural effusion | 7 | 3.6 | 1.5-7.3 |
| Central nervous system | 5 | 2.6 | 0.8-5.9 |
| Others | 4 | 2.1 | |
| *Evolution* | | | |
| ICU transfer | 15 | 7.8 | 4.4-12.5 |
| Death | 14 | 7.3 | 4.0-11.9 |

95% CI: 95% confidence interval; ICU: intensive care unit.

Regarding the CBC, anemia was observed in 45.0% of the cases (95% CI: 37.8-52.4), and the mean lowest hemoglobin level of all patients who received any type of transfusion during hospitalization was 9.0 g/dL. Eosinophilia was observed in 17.6% of the cases (95% CI: 12.5-23.9).

Several platelet counts were performed for each patient during hospitalization. A mean platelet count of 26.4 x $10^9$/L (95% CI: 23.7-29.1 × $10^9$/L), with a minimum value < 1 × $10^9$/L of blood was observed when the lowest values for each patient were considered. The mean platelet count upon hospital discharge was 111.2 × $10^9$/L (95% CI: 97.8-124.7 × $10^9$/L). The mean lowest leukocyte count was 4.6 × $10^9$/L (95% CI: 3.8-5.3 × $10^9$/L), with a minimum value of 0.7 x $10^9$/L and a maximum value of 57.0 × $10^9$/L (Table 3).

The mean AST level was 309.7 IU/L (95% CI: 140.7-478.7 IU/L), with minimum and maximum values of 18 and 6,390 IU/L, respectively. For alanine aminotransferase (ALT), the mean value was 167.6 IU/L (95% CI: 105.6-229.7 IU/L), with minimum and maximum values of 21 and 2,296 IU/L, respectively (Table 3).

Table 4 shows usage of blood component transfusions. In this study, 32.1% of all patients received some type of transfusion. Of those, 10.9% received only platelet concentrate, 9.8% received only FFP and 11.4% received both blood components.

**Table 3 - Description of hematic characteristics of patients with dengue hemorrhagic fever in the city of Rio Branco, Acre from January 2007 to May 2011.**

| Variable | n | % | | 95% CI |
|---|---|---|---|---|
| *Anemia*[a] | 86 | 45.0 | | 37.8-52.4 |
| *Eosinophilia*[b] | 33 | 17.6 | | 12.5-23.9 |
| | Mean | SD | Median | (95% CI) |
| *Platelets (×10$^9$/L)* | | | | |
| At discharge | 111.2 | 82.8 | 88.0 | 97.8-124.7 |
| Lowest | 26.4 | 17.4 | 21.8 | 23.7-29.1 |
| *Leucocytes (×10$^9$/L)* | | | | |
| Lowest count | 4.6 | 5.0 | 3.5 | 3.8-5.3 |
| *Transaminases* | | | | |
| AST (IU/L) | 309.7 | 788.2 | 174 | 140.7-478.7 |
| ALT (IU/L) | 167.6 | 287.7 | 99 | 105.6-229.7 |

95% CI: 95% confidence interval; AST: aspartate transaminase; ALT: alanine aminotransferase.
[a] There was no erythrogram value for one patient.
[b] There were no eosinophil values for eight patients.

**Table 4 - Blood component transfusion characteristics of patients with dengue hemorrhagic fever in the city of Rio Branco, Acre, from January 2007 to May 2011.**

| Variable | n | % | 95% CI |
|---|---|---|---|
| *Transfusions by patient* | | | |
| No | 131 | | |
| Yes | 62 | 32.1 | 25.6-39.2 |
| *Blood component transfused* | | | |
| Platelet concentrate | 21 | 10.9 | 6.9-16.2 |
| FFP | 19 | 9.8 | 6.0-14.9 |
| Platelet concentrate and FFP | 22 | 11.4 | 7.3-16.7 |
| *Transfusions by blood component* | | | |
| Platelet concentrate | 43 | 22.3 | 16.6-28.8 |
| FFP | 41 | 21.2 | 15.7-27.7 |
| Packed red blood cells | 5 | 2.6 | 0.8-5.9 |

95% CI: 95% confidence interval; FFP: fresh frozen plasma.

Regarding transfusions in reference to the type of blood component and transfusion reaction, the following results were observed: platelet concentrate was administered to 22.3% of the patients with 7.1% exhibiting transfusion reactions, and FFP was administered to 21.2% with 2.5% exhibiting transfusion reactions. Only 2.6% of the patients received packed red blood cells, and none reported transfusion reactions (Table 4). Of the four patients who received platelets or FFP and exhibited transfusion reactions, two had allergic reactions; the types of transfusion reactions were not described for the other patients.

Of the 43 patients who received platelet concentrate, a mean of 7.5 IU of platelet concentrate was infused per patient with a median of 6 IU per patient. Of the 41 patients who received FFP, a mean of 5.2 IU were infused per patient with a median of 4 IU per patient. Only five patients received packed red blood cells, with an infusion mean of 3.2 IU per patient and a median of 3 IU per patient.

Additionally, 12.9% (8/62) of the patients who received FFP and/or platelet transfusions evolved to death, compared with 4.6% (6/131) of those who did not receive transfusions. This high mortality rate associated with transfusion was statistically significant (p-value = 0.037).

## Discussion

Dengue is an infectious disease with persistent occurrence, especially in developing countries. Despite recent economic growth, success in controlling this disease has not been achieved, and dengue has evolved from cyclic epidemic outbreaks to a lack of seasonality, given the increase in new and relapsed cases. All of these factors have contributed to the rise in frequency of complications and the development of severe disease forms. The lack of technical support and scientific basis for the proper management of cases with hemorrhagic manifestations, especially regarding transfusion procedures, might contribute to the occurrence of death in potentially avoidable cases.

Females were predominant in this study, accounting for 57% cases in comparison to the 48% reported in Indonesia.[13] The mean patient age in our study was 38.2 years (95% CI: 35.3-41.2 years), higher than that reported by Brito[14] in 2007 for a 13-year period in Brazil and for a 25-year period in India.[15] These differences in age groups can be attributed to the case selection criteria and the types of existing coverage in the hospitals where the studies were conducted.

On assessing the distributions of observed clinical manifestations, fever and headache were the most frequent, results that are in agreement with several studies in the literature.

The analysis of bleeding manifestations in this sample, the magnitude of its occurrence was higher compared to that reported in the literature. In this study, bleeding occurred in 35.8% of cases most commonly displayed as petechiae, gingival bleeding and epistaxis. In Thailand, the occurrence of hemorrhagic manifestations was reported in 50.2% of 175 pediatric patients, and these cases included hematemesis in addition to petechiae and epistaxis.[16] In Indonesia, bleeding occurred in 6% of the cases with gastrointestinal sites being the most common.[13] Another study from India reported that 15.1% of patients exhibited bleeding, with petechiae (9.3%) and epistaxis (2.7%).[11] Despite the concern of hemorrhagic manifestations, Chaudhary et al. concluded that there was no correlation between hemorrhagic manifestations and serum platelet counts.[15] These data from the literature hinder a better comparison of results, mainly due to differences in the patient selection criteria.

The occurrence of hematocrit changes in this study also differed from those reported in the literature. In the

present study, 45% of patients had anemia at some point during hospitalization. In 2006, Chaudhary et al. reported a mean hematocrit of 35.4%.[15] Collection of the mean erythrocyte parameters only upon admission is insufficient since hematocrit variations can occur as a result of the hydroelectrolytic status during patient hospitalization or because of bleeding that can lead to a reduced hematocrit.

In Brazil, changes in transaminases have been described in more than 80% of the cases,[14] a rate similar to that observed in this study, in which 95% of the cases had AST levels ranging from 140.7-478.7 IU/L and ALT levels ranging from 105.6-229.7 IU/L. These results demonstrate the importance of laboratory assessment upon admission and during hospitalization. Additionally, there is evidence of a correlation between the increase in these parameters and mortality. An association of these test results with liver dysfunction and acquired coagulopathy should be considered as an indication of the need to monitor the coagulation status and FFP transfusions.

In Thailand, 10.6% of patients with dengue hemorrhagic fever received some form of transfusion, and 6.9% of these received platelet concentrate, 5% received FFP and 3.1% received packed red blood cells.[16] In India, a group of patients received platelet concentrate; among these cases, 31.8% were considered inappropriate transfusions and 26.9% received FFP.[15]

In Singapore, 12.6% of patients received platelet transfusions.[12] In India, 42.6% of patients received platelet concentrates, 5% received plasma and 2.2% received packed red blood cells.[11] In Indonesia, platelet concentrate transfusions were performed in 12% of cases, with no significant difference in the incidence of hemorrhagic manifestations when compared with the group that did not receive platelet transfusions, even in patients with platelet counts < 25.0 × $10^9$/L.[13] However, this study also showed that 56.5% of patients who received platelet concentrate transfusions had platelet counts higher than 100.0 × $10^9$/L and 1.4% presented some type of bleeding.

In the present study, 32.1% of patients received some form of transfusion; 22.3% of those patients received platelet concentrate, 21.2% received FFP and only 2.6% received packed red blood cells.

In an observational study of dengue patients in Martinique, several received platelet concentrate transfusions. Of the 350 evaluated cases, 9 (2.6%) received platelet transfusions, with a mean of 3.66 IU per patient (range: 2.8-13.2 IU), 3 (8.6%) received packed red blood cells and 2 (0.6%) received FFP.[17] In India, 3.4 IU of platelet concentrate were infused per patient,[15] a substantially smaller volume than that documented in our study (7.5 IU per patient).

The reported mortality in a study from Thailand was 1.14%,[16] while mortality rates in Martinique and India were less than 1%[17] and 2%, respectively;[14] all of these rates were lower than the 7.3%, observed in this study. The presence of bleeding or clinical severity increases the indication for transfusions, and the indicators of plasma leakage and elevated transaminase levels might be related to increased mortality.

The apparent association of plasma and platelet concentrate transfusions with death requires a better evaluation because there is a possibility that these patients evolved with more severe clinical conditions that might explain the higher mortality in this group and why transfusion could not change the outcome.

## Conclusion

The distribution patterns of clinical and laboratory criteria observed did not differ substantially from those described in the literature, despite the differences in sample selection criteria between studies. The clinical profile of the patients in our study can be characterized by the presence of fever, headache and myalgia; with petechiae, gingival bleeding and epistaxis as the most frequent sites of bleeding. Regarding the erythrocyte parameters, anemia was a frequent finding and the mean of the lowest platelet count for each patient upon admission was 26.4 × $10^9$/L. Transaminases were elevated in most patients. Cardiorespiratory dysfunction was the most frequently observed complication.

Transfusion was used as part of the treatment regimen for dengue hemorrhagic fever in one-third of the cases, with a mixed platelet concentrate and plasma transfusion applied in approximately 10% of the cases. In our study, the use of transfusion therapy did not reduce mortality with death occurring in 7.3% of the cases. The results of this study suggest the need for more appropriate studies to assess survival in a cohort of patients with severe dengue and hemorrhagic manifestations.

## Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. Singhi S, Kissoon N, Bansal A. Dengue and dengue hemorrhagic fever: management issues in an intensive care unit. J Pediatr (Rio J). 2007;83(2 Suppl):S22-35.
2. Brasil - Dengue: diagnóstico e manejo clínico – Adulto e Criança. 3rd ed. - Brasília: Séria A. Normas e Manuais Técnicos; 2007.
3. Halstead SB. Dengue in the Americas and Southeast Asia: Do they differ? Rev Panam Salud Publica. 2006;20:407-15.
4. Nogueira RM, Araujo JM, Schatzmayr HG. Dengue viruses in Brazil, 1986-2006. Rev Panam Salud Publica. 2007;22:358-63.
5. Sistema de Informação de Agravos de Notificação – Sinan / Datasus / Ministério da Saúde – avaliable from: http://dtr2004.saude.gov.br/sinanweb/tabnet/tabnet?sinannet/dengue/ bases/denguebrnet.def.
6. Lupi, O, Carneiro CG, Coelho IC. Manifestações mucocutâneas da dengue. An Bras Dermatol. 2007;82:291-305.
7. Sellahewa KH, Samaraweera N, Thusita KP, Fernando JL. Is fresh frozen plasma effective for thrombocytopenia in adults with dengue fever? A prospective randomised double blind controlled study. Ceylon Med J. 2008;53:36-40.

8. Kabra SK, Madhulika YJ, Tripathi P, Singhal T, Broor S, Dar L, et al. Role of platelet transfusion in dengue hemorrhagic fever. Indian Pediatr. 1998;35:452-5.
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;35:277-85.
10. Sellahewa KH. Dengue fever – predictors of disease severity and their influence on management. Ceylon Med J. 2008;53:75-8.
11. Makroo RN, Vaina V, Kumar P, Kanth RK. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital. Asian J Transfus Sci. 2007;1:4-7.
12. Lye DC, Lee VJ, Sun Y, Leo YS. Lack of efficacy of prophylactic platelet transfusion for severe thrombocytopenia in adults with acute uncomplicated dengue infection. Clin Infect Dis. 2009;48:1262-5.
13. Chairulfatah A, Setiabudi D, Agoes R, Colebunders R. Thrombocytopenia and Platelet Transfusions in Dengue Haemorrhagic Fever and Dengue Shock Syndrome. Dengue Bulletin. 2003;27:138-43.
14. Brito CA. Dengue: perfil clínicoepidemiológico, laboratorial e avaliação de fatores de risco em uma coorte prospectiva entre pacientes adultos em Recife, Nordeste do Brasil. [thesis]. Recife: Fundação Oswaldo Cruz; 2007.
15. Chaudhary R, Khetan D, Sinha S, Sinha P, Sonker A, Pandey P, et al. Transfusion support to Dengue patients in a Hospital based blood transfusion service in north India. Transfus Apher Sci. 2006;35:239-44.
16. Chuansumrit A, Phimolthares V, Tardtong P, Tapaneya-Olarn C, Tapaneya-Olarn W, Kowsathit P, et al. Transfusion requirements in patients with dengue hemorrhagic fever. Southeast Asian J Trop Med Public Health. 2000;31:10-4.
17. Thomas L, Kaidomar S, Kerob-Bauchet B, Moravie V, Brouste Y, King JP, et al. Prospective observational study of low thresholds for platelet transfusions in adult dengue patients. Transfusion. 2009;49:1400-11.