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Original Article

# Factors associated with shock in children with dengue hemorrhagic fever

Erick F Kan, MD; TH Rampengan, MD

**ABSTRACT**

***Background*** Shock in dengue hemorrhagic fever (DHF) still constitutes an important problem in children. Predicting DHF patients who will develop shock is difficult.

***Objective*** The aim of this study was to find out factors associated with shock in DHF.

***Methods*** This was a prospective observational study. Subjects were children hospitalized from April to July 2000 who met the WHO criteria for DHF and had positive serological confirmation. Association between independent variables (age, gender, duration of fever, abdominal pain, vomiting, hepatomegaly, platelet count, hematocrit level, and nutritional status) and the dependent variable (shock) was analyzed by logistic regression model..

***Results*** There were 85 children who met the eligibility criteria consisting of 50 (59%) boys and 35 (41%) girls with an average age of 7.1 years (SD 2.88). Shock occurred in 42 (49%) children. Of the 42 children with shock, the age group of 5-9 years made up the biggest group (57%) consisting of 23 (55%) boys and 19 (45%) girls. Hepatomegaly was found in 32 (76%) children, abdominal pain and vomiting in 30 (71%) and 36 (86%) children, respectively, and good nutrition in 22 (52%) children. Shock occurred mainly on the fourth and fifth days (76%). Almost half of the patients (45% and 52%) had hematocrit level of 46-50% and platelet count of 20,000-50,000/ml, respectively. By logistic regression analysis, it was found that duration of fever, abdominal pain, hematocrit level, and platelet count constituted independent factors correlating with shock in DHF.

***Conclusion*** Abdominal pain, fever lasting four to five days, hematocrit level of ≥46%, and platelet count of ≤50,000/µl were associated with shock in DHF **[Paediatr Indones 2004;44:171-175].**

***Keywords:*** *dengue hemorrhagic fever, shock, associated factors*

Dengue hemorrhagic fever (DHF) associated with shock is still a serious problem in children.[1] The number of DHF patients who experience shock varies. Rampengan (1986) in Manado reported that the occurrence of shock in DHF was about 60% of all patients with a mortality rate of 6.6%.[2] Hadinegoro reported that the prevalence of DHF with shock in almost all hospitals in Indonesia was 16-40% with a mortality rate between 5.7 and 50%.[3] DHF is also one of the public health problems in Manado City, although the national mortality rate of DHF has decreased. So far, an increasing number of DHF patients were observed in Malalayang Hospital, Manado accompanied by an increase in mortality rate.[4,5] Most of the deaths were caused by shock and recurrent shock.[5]

Predicting DHF patients who will develop shock or recurrent shock is not easy.[1,6] The clinical manifestations of DHF vary considerably, while the pathogenesis is not known exactly and different types of viruses were established in the various places. Besides, many factors influence the development of shock. The need for early anticipation of shock has led the authors to identify factors associated with shock in DHF in Malalayang Hospital, Manado.

From the Department of Child Health, Medical School, Sam Ratulangi University, Manado, Indonesia.

**Request reprints to:** TH Rampengan, MD, Department of Child Health, Medical School, Sam Ratulangi University, Malalayang Hospital, Manado, Indonesia. Tel. 62-431-53191, Fax. 62-431-859091.

## Methods

This observational study was conducted in April-September 2000 at the Department of Child Health, Medical School, Malalayang Hospital, Manado. All hospitalized patients who met the WHO criteria for DHF (1997)[7] and had positive serological confirmation by ELISA method were included. Patients were excluded from the study if they had any other infectious disease or their parents did not give informed consent. The dependent variable was shock and the independent variables were age, sex, duration of fever, vomiting, abdominal pain, hepatomegaly, hematocrit level, platelet count, and nutritional status.

Subjects were divided according to the clinical severity of the disease i.e., DHF grade I without shock, grade II without shock, grade III with shock, and grade IV with shock. From every subject, a history was obtained, including duration of fever, the presence of abdominal pain, vomiting, bleeding, and shock. Physical examination was done daily to recognize any sign of shock, bleeding manifestations, and hepatomegaly. The anthropometric examination to determine nutritional status was done using the weight for age parameter according to WHO-NCHS standard.

The highest value of hematocrit levels examined by microhematocrit every 4-6 hours was taken. Platelet count by indirect method was performed daily and the lowest value was recorded. Serological testing (ELISA method) using single sample on acute phase and virus typing by PCR were done in collaboration with *LITBANGKES* (National Agency for Health Research and Development), Jakarta.

Logistic regression analysis was performed to evaluate the relationship between the independent variables and the dependent variable. SPSS version 9 was used for analyses. A *p* value of less than 0.05 was considered significant.

## Results

During the study period, 117 children with suspected DHF were admitted to Malalayang Hospital. From these 117 children, five were excluded because they did not fulfill the eligibility criteria, and 27 due to negative serologic test. Finally, 85 children participated in the study; the youngest was 2.3 years old and the oldest was 12.8 years old with an average of 7.1 years (SD 2.88). The number of boys was 50 (59%) and the number of girls was 35 (41%), giving a sex ratio of 1.4:1. Most of the patients were admitted on the fourth or fifth day of fever (range: 1-6 days, average: 3.8 days; SD 1.16). Shock was found in 42 (49%) children.

Serological examination revealed that 57 (67%) children suffered from secondary dengue infection, while 28 (33%) suffered from primary dengue infection. The examination of virus type was only done in 62 patients; only virus type 1 (n=5) and type 2 (n=6) were found **(Table 1)**.

**TABLE 1.** THE CHARACTERISTICS AND CLINICAL MANIFESTATIONS OF DHF PATIENTS

| Characteristics | Number | Percentage |
|---|---|---|
| **Age** | | |
| <1 year | 0 | 0 |
| 1-4 years | 24 | 28 |
| 5-9 years | 44 | 52 |
| ≥10 years | 17 | 20 |
| **Sex** | | |
| Male | 50 | 59 |
| Female | 35 | 41 |
| **Nutritional Status** | | |
| Overweight | 11 | 13 |
| Normal | 43 | 51 |
| Underweight | 31 | 36 |
| **Duration of fever** | | |
| <4 days | 29 | 34 |
| 4-5 days | 51 | 60 |
| >5 days | 5 | 6 |
| **Shock** | 42 | 49 |
| **Hepatomegaly** | 55 | 65 |
| **Antibody response** | | |
| Primary infection | 28 | 33 |
| Secondary infection | 57 | 67 |
| **Serotype of virus*** | | |
| Den-1 | 5 | |
| Den-2 | 6 | |

*Obtained in 62 samples

From the 42 children who develop shock, most were 5-9 years old and boys outnumbered girls (55% vs. 45%). DHF with shock was predominantly seen in patients with fever on the fourth and fifth day (76%). Hepatomegaly, vomiting, and abdominal pain occurred in 76%, 71%, and 86% of DHF patients with shock, respectively **(Table 2).**

**TABLE 2.** FACTORS ASSOCIATED WITH DHF AND SHOCK

| Characteristics | Shock (n=42) | No Shock (n=43) |
|---|---|---|
| **Age** | | |
| <1 year | 0 | 0 |
| 1-4 years | 11 (26%) | 13 (30%) |
| 5-9 years | 24 (57%) | 20 (47%) |
| ≥10 years | 7 (17%) | 10 (23%) |
| **Sex** | | |
| Male | 23 (55%) | 27 (63%) |
| Female | 19 (45%) | 16 (37%) |
| **Nutritional status** | | |
| Overweight | 5 (12%) | 6 (14%) |
| Normal | 22 (52%) | 21 (49%) |
| Underweight | 15 (36%) | 16 (37%) |
| **Duration of fever** | | |
| <4 days | 7 (17%) | 22 (51%) |
| 4-5 days | 32 (76%) | 19 (44%) |
| >5 days | 3 ( 7% ) | 2 (5% ) |
| **Hepatomegaly** | 32 (76%) | 23 (53%) |
| **Abdominal pain** | 36 (86%) | 15 (35%) |
| **Vomiting** | 30 (71%) | 23 (53%) |
| **Hematocrit level (vol%)** | | |
| <46 | 10 (24%) | 25 (58%) |
| 46-50 | 19 (45%) | 17 (40%) |
| >50 | 13 (31%) | 1 (2% ) |
| **Platelet count (/µl)** | | |
| <20,000 | 9 (21%) | 1 (2% ) |
| 20,000-50,000 | 22 (52%) | 15 (35%) |
| >50,000 | 11 (26%) | 27 (63%) |

On logistic regression analysis using stepwise procedure, it was found that independent associated factors of the occurrence of shock in DHF were duration of fever, abdominal pain, hematocrit level, and platelet count **(Table 3).**

**TABLE 3.** LOGISTIC REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH DHF AND SHOCK

| Variables | Coefficient (B) | Standard Error (SE) | df | Sig |
|---|---|---|---|---|
| Sex | -0.4130 | 0.8081 | 1 | 0.6093 |
| Abdominal pain | 2.3325 | 0.8912 | 1 | 0.0089* |
| Vomiting | 1.1181 | 0.8912 | 1 | 0.2277 |
| Nutritional status | -0.0309 | 0.0204 | 1 | 0.1295 |
| Platelet count | -7.1E-05 | 2.394E-05 | 1 | 0.0032* |
| Hematocrit level | 0.4691 | 0.1683 | 1 | 0.0053* |
| Hepatomegaly | -0.0117 | 0.9371 | 1 | 0.9900 |
| Duration of fever | 1.8274 | 0.5324 | 1 | 0.0006* |
| Age | -0.2147 | 0.1426 | 1 | 0.1323 |
| Constant | -23.6023 | 8.1240 | 1 | 0.0037 |

* p<0.05

## Discussion

This study was limited to patients who met the WHO criteria for DHF (1997) confirmed by ELISA serologic test using single sample in acute phase. There was no double serum (acute and convalescent) and HI examinations in this study due to limited facilities.

We found that children aged 5-9 years were most sensitive to infection of dengue virus. It was different from Rampengan's study in 1986 that reported younger age range (4-6 years). This difference may be caused by the alteration of transmission setting. In the beginning era of DHF, the transmission generally took place at home, but at present it has shifted to public facilities, such as schools, mosques, churches, and children's playgrounds.[8] This was supported by the study of Soegiyanto *et al*[9] in which of the patients who were treated in the hospital, 72% were schoolchildren and only 28% were under-five years old. Health authorities must be aware of this phenomenon to improve their efforts in preventing dengue infection.

The sex distribution in this study showed that boys were more sensitive to dengue infection than girls. This was in accord with the reports of Soegiyanto[9] and Lum[10] but different from some previous studies.[2,3,11,12] Boys are more prone because they go to public places more often than girls do, thus the opportunity to be infected by the dengue virus becomes higher.[9]

According to the severity of the disease, it was clear that the number of patients with shock almost equaled those without. The high prevalence of shock in DHF patients shows that the health authority has not yet succeeded in disseminating information to the society to get immediate treatment for DHF.[8]

Data from a virology survey in Manado in an outbreak in the year of 1999-2000 showed that dengue virus types 2 and 4 were dominant. Children infected with type 2 virus were more prone to develop shock (unpublished data). Our study found only dengue virus types 1 and 2, possibly because of the small number of subjects. It is known that all virus types exist in Indonesia and can cause fatal disease.[11,13] Soe *et al* found that children with secondary infection are more prone to develop shock than those with primary infection.[14]

From the 42 DHF children with shock, the age group of 5-9 years, male sex, fever lasting for 4-5 days, good nutritional status, hematocrit level of 46-50 vol%, and platelet count of 20,000-50,000/µl were dominant. Other clinical signs which were also promi-

nent were hepatomegaly, vomiting, and abdominal pain. The symptoms and clinical signs reported varies in many areas; it is supposed that the strain or serotype of virus can influence symptoms and clinical signs occurring in DHF with shock.[14] By logistic regression analysis, it was found that factors associated with shock in DHF were abdominal pain, duration of fever, hematocrit level, and platelet count.

Abdominal pain is a prominent clinical manifestation of DHF infection which is not included in the WHO criteria. Almost all countries in South East Asia reported this symptom with high frequency. Lum and friends[10] assumed that abdominal pain in DHF patients should be considered as a sign of gastrointestinal bleeding. Histopathological examination of digestive tract shows edema and bleeding in the mucosa, submucosa, and serous membrane of DHF patients with abdominal pain.[16] Bleeding and anorexia in these patients can cause shock.

The time of hospital admission has significant relation with shock in DHF. It seems that the earlier a patient goes to the hospital, the risk for the occurrence of complicated disease is less.[2,3,17]

The increase of hematocrit level seemed to have significant relation with shock in DHF. Increased hematocrit level indicates continuous plasma leakage causing more severe hypovolemia.[18]

Low platelet count is a sign for the occurrence of shock in DHF. Platelets are a secretor cells that has granules containing all kinds of mediators. Endothelial damage will create platelet aggregation and the activated platelet will release histamine-like substance and 5-hydroxytryptamine that may increase vascular permeability.[19] This study found that low platelet count had relationship with shock in DHF.

In conclusion, abdominal pain, fever lasting for four to five day, hematocrit level of $\leq$46%, and platelet count of $\geq$50,000/$\mu$L were associated with shock in DHF.

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