

# CLINICAL CHARACTERISTICS OF SEVERE DENGUE IN CHILDREN DURING 2017 OUTBREAK

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## Summary

**Objective:** To study the clinical features of severe dengue in children during the 2017 outbreak, at the National Hospital for Tropical Diseases. **Subjects and Methods:** Retrospective study on all children diagnosed with severe dengue. **Results:** The proportion of children classified with severe dengue was 6.6% (49/742). Among the categories of severe dengue, severe plasma leakage (shock or fluid accumulation with respiratory distress) was 42.9% (21/49), severe organ impairment 30.6% (15/49) and severe bleeding 26.5% (13/49). Ratio of men/women = 1.04/1, with background disease 4.1%. The age group > 12 ÷ ≤18 years accounts for the highest proportion (63.3%), followed by > 5 ÷ ≤ 12 years (32.7%) and the age from 13 to 60 months (4.1%). The most common clinical manifestations were hemorrhage (79.5%), fever > 39°C (51%), nausea or vomiting (48.9%) and abdominal pain (44.9%). Hematocrit > 0.42 l/l (71.4%); platelet < 50G/l (77.5%), the rate of AST ≥ 1000U/l was 12.2%, ALT ≥ 1000U/l was 8.2%, acute renal failure 18.3%. Two deaths were associated with shock and severe organ impairment. **Conclusion:** In the 2017 outbreak, in children with severe dengue, there were 3 clinical manifestations (severe plasma leakage, severe organ impairment, severe bleeding). The rate of severe organ impairment is more common than in previous outbreaks. Shock patients present with severe organ failure and vice versa. Further studies are needed to evaluate severe organ impairment in children.

**Key words:** severe dengue, children, clinical, subclinical, DHF.

## INTRODUCTION

Dengue hemorrhagic fever (DHF) is an acute infectious epidemic disease caused by four types of *Dengue* virus. Currently, DHF has become one of the top 10 causes of hospitalization and mortality in children in Southeast Asia. According to the WHO reports, in the period 2004 ÷ 2010, Vietnam is the third country with number of dengue cases in 30 most highly endemic countries<sup>[10,6,9]</sup>. The mortality rate of dengue disease is estimated 2 ± 5% associ-

ated with the clinical manifestations of severe dengue and can reach up to 20% if left untreated<sup>[6,9]</sup>.

In Vietnam, DHF has become a local epidemic. Although, the Ministry of Health has implemented prevention programs, contributing to reducing the death rate of the disease, but the incidence rate has not decreased, and major epidemics still repeat in about 3 to 5 years<sup>[2]</sup>. In 2017, a dengue outbreak occurred in the whole country with many severe cases and deaths<sup>[2]</sup>. In order to help early detection and timely treatment to reduce the mortality of the disease, we conduct research: describe some clinical and subclinical characteristics of severe dengue in children in the 2017 outbreak.

## SUBJECTS AND METHODS

**Subjects:** Including pediatric patients diagnosed with severe dengue, treated at the National Hospital for Tropical

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Diseases, from January 1, 2017 to December 31, 2017.

**Criteria for selecting patients to study:** According to the clinical diagnostic criteria of the Ministry of Health and having dengue NS1(+) antigen results, or ELISA test to detect IgM(+), or PCR(+). The classification criteria of Dengue ± warning signs and severe dengue are based on the "Guidelines for diagnosis and treatment of dengue" of the Ministry of Health in 2011<sup>[1]</sup>. Criteria for diagnosis of acute renal failure are based on the "Guidelines for diagnosis and treatment of some kidney - urinary diseases" of the Ministry of Health in 2015<sup>[3]</sup>.

**Sample size and sampling method:** In this study, we do not calculate the sample size. All patients who met the study criteria were selected for analysis.

#### Data collection and processing

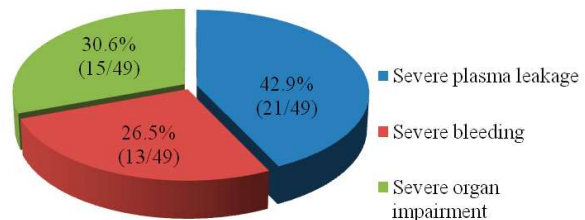
- Collect research data: each patient has its own medical record, according to a unified form.

- Data management and processing: using SPSS Statistic 20 software.

- The data will be processed according to medical statistics method.

## RESULTS

During the 2017 outbreak, we identified 49/742 (6.6%) children classified as severe dengue. The clinical manifestations of 49 children with severe dengue were presented in graph 1.



**Graph 1. Distribution of patients according to clinical manifestations**

*Comment:* Among children classified as severe dengue, severe plasma leakage accounted for the highest proportion (42.9%), followed by severe organ impairment (30.6%) and severe bleeding (26.5%). In 15 children with severe organ involvement, 8 were identified with acute renal failure, 6 children with severe liver failure and 01 child with acute respiratory failure.

**Table 1. Some epidemiological characteristics of children with severe dengue**

Epidemiology characteristics	Severe plasma leakage (n = 21)	Severe organ involvement (n = 15)	Severe bleeding (n = 13)	Total (ratio %)
	n (%)	n (%)	n (%)	49 (100%)
<b>Age</b>				
≤ 12 months	0 (0%)	0 (0%)	0 (0%)	0 (0%)
13 ÷ ≤ 60 months	2 (9.5%)	0 (0%)	0 (0%)	2 (4.1%)
> 5 ÷ ≤ 12 years	11 (52.4%)	3 (20%)	2 (15.4%)	16 (32.6%)
> 12 ÷ 18 years	8 (38.1%)	12 (80%)	11 (84.6%)	31 (63.3%)
<b>Sex</b>				
Male	10 (47.6%)	12 (80%)	3 (23.1%)	25 (51%)
Female	11 (52.4%)	3 (20%)	10 (76.9%)	24 (49%)
<b>Background diseases</b>	1 (4.8%)	1 (6.7%)	0 (0%)	2 (4.1%)

*Comment:* Among children classified as severe dengue, the ratio of male/female = 1.04/1 and 4.1% had background diseases. Severe dengue was more common in the age group > 12 to 18 years old (63.3%), followed by the age from 6 to 12 years old (32.7%) and at the age from 13 to 60 months (4.1%). There was no patient with severe dengue aged less than 12 months.

**Table 2. Some clinical characteristics of children with severe dengue**

Epidemiology characteristics	Severe plasma leakage (n = 21)	Severe organ involvement (n = 15)	Severe bleeding (n = 13)	Total (ratio %)
	n (%)	n (%)	n (%)	49 (100%)
<b>Fever (°C)</b>				
> 39	12 (57.1%)	7 (46.7%)	6 (46.2%)	25 (51%)
37,5 ÷ 39	9 (42.9%)	8 (53.3%)	7 (53.8%)	24 (49%)
<b>Manifestation of hemorrhage</b>				
Petechiae	14 (66.7%)	9 (60%)	6 (46.2%)	29 (59.2%)
Epistaxis	4 (19%)	2 (13.3%)	4 (30.8%)	10 (20.4%)
Gum bleeding	3 (14.3%)	4 (26.7%)	0 (0%)	7 (14.2%)
Gastrointestinal bleeding	3 (14.3%)	3 (20%)	3 (23.1%)	9 (18.3%)
Vaginal bleeding	2 (9.5%)	1 (6.7%)	6 (46.2%)	9 (18.3%)
Hematuria	0 (0%)	1 (6.7%)	1 (7.7%)	2 (4.1%)
<b>Nausea or vomiting</b>				
	11 (52.4%)	8 (53.3%)	5 (38.5%)	24 (48.9%)
<b>Abdominal pain</b>				
	11 (52.4%)	5 (33.3%)	6 (46.2%)	22 (44.9%)
<b>Diarhea</b>				
	4 (19%)	8 (53.3%)	2 (15.4%)	14 (28.6%)
<b>Hepatomegaly &gt; 2 cm</b>				
	2 (9.5%)	0 (0%)	1 (7.7%)	3 (6.1%)
<b>Severe organ impairment</b>				
Liver	0 (0%)	6 (40%)	0 (0%)	6 (12.2%)
Kidney	1 (4.8%)	8 (53.3%)	0 (0%)	9 (18.3%)
Respiratory	0 (0%)	1 (6.7%)	0 (0%)	1 (2%)
<b>Shock</b>				
	21 (100%)	2 (13.3%)	0 (0%)	23 (32.6%)
<b>Fatality</b>				
	1 (4.8%)	1 (6.7%)	0 (0%)	2 (4.1%)

Comment: The manifestations of fever, hemorrhage, nausea or vomiting, and abdominal pain were evenly distributed in all 3 major clinical categories. Among children classified as severe plasma leakage, 01 child was identified

with acute renal failure and in 15 children with severe organ impairment, 2 children developed shock syndrome. Two deaths related to shock and severe organ impairment.

**Table 3. Subclinical characteristics of children with severe dengue**

Subclinical characteristics	Severe plasma leakage (n = 21)	Severe organ involvement (n = 15)	Severe bleeding (n = 13)	Total (ratio %)
	n (%)	n (%)	n (%)	49 (100%)
<b>Hematocrit (l/l)</b>				
< 0.42	3 (14.3%)	3 (20%)	8 (61.5%)	14 (28.6%)
0.42 ÷ 0.45	4 (19%)	2 (13.3%)	2 (15.4%)	8 (16.3%)
> 0.45	14 (66.7%)	10 (66.7%)	4 (30.8%)	27 (55.1%)
<b>Platelets (G/l)</b>				
< 50	18 (85.7%)	10 (66.7%)	10 (76.9%)	38 (77.6%)
50 ÷ 100	3 (14.3%)	4 (26.7%)	3 (23.1%)	10 (20.4%)
> 100	0 (0%)	1 (6.7%)	0 (0%)	1 (2%)
<b>ALT (U/L)</b>				
≤ 40	4 (19%)	2 (13.3%)	7 (53.8%)	13 (26.5%)
41 ÷ 200	14 (66.7%)	6 (40%)	5 (38.5%)	25 (51%)
201 ÷ 999	3 (14.3%)	3 (20%)	1 (7.7%)	7 (14.3%)
≥ 1000	0 (0%)	4 (26.7%)	0 (0%)	4 (8.2%)

Subclinical characteristics	Severe plasma leakage (n = 21)	Severe organ involvement (n = 15)	Severe bleeding (n = 13)	Total (ratio %)
	n (%)	n (%)	n (%)	49 (100%)
<b>AST (U/L)</b>				
≤ 40	1 (4.8%)	2 (13.3%)	2 (15.4%)	5 (10.2%)
41 ÷ 200	12 (57.1%)	3 (20%)	10 (76.9%)	25 (51%)
201 ÷ 999	8 (38.1%)	4 (26.7%)	1 (7.7%)	13 (26.6%)
≥ 1000	0 (2%)	6 (40%)	0 (0%)	6 (12.2%)
<b>Acute renal failure</b>	1 (4.8%)	8 (53.3%)	0 (0%)	9 (18.3%)

*Comment:* Of the children classified as severe dengue, 71.4% had a plasma drainage (hematocrit  $\geq 0.42$  l/l), and 77.6% had a severely reduced platelet count ( $< 50$  G/l). The ratio of enzyme AST  $\geq 1000$  U/l was 12.2% and ALT  $\geq 1000$  U/l was 8.2%. The rate of acute renal failure was 18.3%.

## DISCUSSION

Our research results show that, in the 2017 dengue epidemic, the rate of children classified as severe dengue accounted for 6.6% of the total number of children admitted to treatment at the National Hospital for Tropical Diseases. This rate is lower than the research result of previous outbreaks in Vietnam, with the shock rate of 18%<sup>[5]</sup> and also lower than the study result of Khansoudaphone Phakhounthong (rate of dengue with the shock is 19.2%)<sup>[7]</sup>. However, the above results only mention severe dengue patients with shock, but do not mention other serious complications, such as severe organ impairment and severe bleeding. According to a study by P. Sreenivasan (2019) in children with severe dengue, shock is still the main cause (accounting for 89.2%), while the rate of organ impairment is 18.3% and severe bleeding is 5.4%<sup>[8]</sup>. During this outbreak, we found that severe organ impairment (30.6%) and heavy hemorrhage (26.5%) accounted for a high proportion among patients with severe dengue, which were uncommon complications in previous outbreaks. here (see graph 1). Compare with studies in adults, according to C.C. Ming (research in Taiwan - China) with severe organ impairment also accounts for a high rate of 41.3%<sup>[4]</sup>. Thus, in the 2017 dengue endemic in Vietnam, although the rate of severe dengue in children was not high, serious complications such as severe organ impairment and severe bleeding have become a problem.

Based on the results of classification of severe dengue (severe plasma leakage, severe organ impairment and severe bleeding), we found no difference in the distribution of the background diseases, nor the sex. The rate of severe plasma leakage is similar in boys and girls, boys have a higher rate of severe organ failure, while girls experience severe bleeding (see table 1). In this study, severe dengue was not seen at the age of less than 1 year, but shock was noted mainly in children aged 6 to 12 years, while severe organ impairment and severe bleeding were seen in children aged  $> 12 \div 18$  years old.

Clinically, symptoms of fever  $\geq 39^\circ\text{C}$ , abdominal pain, nausea or vomiting corresponding to 51%, 44.9% and 48.9% are common symptoms in dengue, as well as common in the early stages of severe dengue (warning signs). In addition, we also found that abdominal pain and nausea or vomiting are common symptoms in patients with severe plasma leakage, diarrhea is a common manifestation in patients with organ impairment.

According to the guidelines of the World Health Organization, when hematocrit  $> 0.42$  l/l is evidence of plasma drainage<sup>[9]</sup>. In our study, 71.4% of children in all 3 major categories have a drainage status (see table 3). Similarly, in all 3 major categories there was a decrease in the number of severely reduced platelets  $< 50$  G/l. However, we also found that, in the group of patients with severe plasma leakage, the proportion of patients with plasma drainage and severe reduction in platelet counts was higher than in the other two groups. The increase in transaminases (ALT and AST) is distributed in all 3 severe categories. Severe hepatic impairment is defined when transaminases  $> 1000$  U/L<sup>[1]</sup>, in our study results, the rate is 12.2% for AST and 8.2% for ALT, which is higher compared with the previous research results. According to Phakhounthong (study in Cambodia), patients with ALT  $>$

1000 U/l only met 5.2%<sup>[7]</sup> and P. Sreenivasan (study in India) only met 1.1%<sup>[8]</sup>. Further, in addition to 1 patient with acute renal failure built up after shock syndrome<sup>[9]</sup>, we identified 08 patients qualified for diagnosis of acute renal failure without association with shock, and 01 patient subsequently shock appeared. Among 02 patients with severe organ impairment progressing to shock, 01 patient with acute respiratory failure and 01 patient with acute renal failure.

## CONCLUSION

In conclusion, through research results on severe dengue in children, during the 2017 outbreak, at the National Hospital for Tropical Disease, we conclude that the

rate of severe dengue was 6.6%. Among children classified as severe dengue, the rate of severe plasma leakage was 42.9% (more common in children > 5 ÷ 12 years old), severe organ failure was 30.6% (more common in children > 12 ÷ 18 years old) and severe bleeding was 26.5%. plasma drainage (71.4%), severe thrombocytopenia (77.6%), and increase in transaminases (enzyme AST and ALT > 40U/L) were seen in all 3 severe categories, with acute renal failure 18.3%. In shock patients, severe organ impairment manifest itself and vice versa. Two deaths were associated with shock and severe organ impairment.

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