

Gallbladder Edema in Dengue Hemorrhagic Fever and Its Association with Hematocrite Levels and Type of Infections

Iskandar Zulkarnain

ABSTRACT

Aim: to determine gallbladder edema with type of dengue infection and hematocrite level.

Methods: a retrospective study was performed on 225 cases of DHF admitted from January to December 1997 to determine the association between the type of Dengue infection, hemoconcentration and the presence or absence of gallbladder edema. Primary or secondary types of dengue infection consider to determine the severity and degree of plasma leakage in dengue hemorrhagic fever. The Chi square and Spearman's tests were performed to establish association between variables.

Results: out of 225 cases of DHF, 129 cases were found with the following dengue serology test results: 92 IgM positive and 37 negative. Abdominal ultrasound was performed in 57 cases, revealing gallbladder edema in 17 cases and none in 40 cases. The 57 cases were classified as primary dengue cases (positive IgM), secondary dengue (positive IgM and IgG), or seronegative (negative IgM). Primary dengue was found in 5 cases with gallbladder edema and 15 cases without (25%). In the secondary dengue group, 10 cases were found with gallbladder edema and 8 cases without (55.5%), while in the non-dengue group, there were 2 cases with gallbladder edema and 17 cases without (10.5%). There was association between the development of gallbladder edema and the type of dengue infection ($p=0.010$). Gallbladder edema was more common in secondary dengue (55%). There was a tendency for gallbladder edema in patients with higher increases in hematocrite.

Conclusion: It conclude that gallbladder edema is more common in cases of secondary dengue and that there is a tendency for gallbladder edema with higher increase of hematocrite.

Key words: gallbladder edema, dengue type of infections, hematocrite levels.

Division of Tropical Medicine and Infectious Diseases, Department of Internal Medicine, Faculty of Medicine of The University of Indonesia

INTRODUCTION

Infection by the dengue virus, which belongs to the family of arthropod-borne (Arbo) virus (now known as Flavivirus) is still endemic in Indonesia. Fifty to one hundred million people are estimated to be infected by the virus each year, with fatal incidences occurring in 60,000 cases. The largest number of deaths is among children.¹⁻² Currently, there is a shift in the number of cases, with a more equal distribution among adults and children.

According to the WHO criteria in 1997, dengue hemorrhagic fever (DHF) manifests as fever and thrombocytopenia accompanied with plasma leakage. Plasma leakage may manifest as hemoconcentration or fluid effusion into the serous cavity, including pleural effusion and ascites.³⁻⁴ Primary or secondary types of dengue infection consider to determine the severity and degree of plasma leakage in dengue hemorrhagic fever.

Dyspepsia syndrome (abdominal pain, discomfort and nausea) is one of the most common complain beside fever. One of the possible caused of this symptom is the gastric mucosal and gall bladder congestion caused by the leakage of the plasma. Ultrasound could be helpful to detect pleural effusion, ascites as well as gallbladder edema, which sometimes present on the 5th to 7th day of the fever. There are still no data about the presence of gall bladder edema in dengue hemorrhagic fever and its association with type of dengue infection and hemoconcentration (elevation of hematocrite levels).

METHODS

A retrospective study was performed among 225 cases of suspected DHF admitted to a private hospital during 1 year (January to December 1997), whose medical records were inspected. The case was included in the study if dengue serology and serial hematocrite data were available. Serology was performed using

(Pan-Bio) immunochromatography. The results of the serology testing were presented as positive or negative IgM and IgG. Ultrasound examination was performed on the 5th to 7th day since the development of fever and the thickness of the gallbladder was measured. Gallbladder wall edema is established by ultrasound examination if the wall exceeds 2 mm in thickness at the fundus. The gallbladder is a small organ located at the ventral surface of the liver. The thickness of its wall is more easily seen using ultrasound in a supine and prone left position. According to serology results, they could be classified as primary dengue (IgM positive, IgG negative), secondary dengue (IgM positive, IgG positive) and seronegative (IgM negative). In the case of negative IgM, a repeat serology was performed 1 week afterwards. Elevated hematocrite is calculated based on the difference between the hematocrite level during hospitalization and during the convalescent phase divided by the hematocrite level during the convalescent phase in percentage. Computer analysis using a statistical computer program was performed to establish the association between the variables type of infection, gallbladder edema, and elevated hematocrite. The Chi square and Spearman's tests were performed to establish association between variables.

RESULTS

Out of 129 cases that met the inclusion criteria, 92 cases were found to be IgM positive and 37 cases were IgM negative. Ultrasound was performed on 57 cases with the following results: 17 cases with gall bladder edema and 40 cases without gallbladder edema. In the primary dengue group, 5 cases were found with gallbladder edema out of 20 cases (25%). Among 18 cases of secondary dengue, 10 cases were found with gallbladder edema (55.5%), while in the seronegative group, 2 cases were found with gallbladder edema out of 19 cases (10.5%). Using Chi square, a significant association was found between the type of dengue infection and the development of gallbladder edema ($p=0.010$).

In the case with gallbladder edema, the percentage of hematocrite increase during the acute and convalescent phase data were as follows:

- In the group with primary dengue, out of 5 cases with gallbladder edema, 4 cases demonstrated an increase in hematocrite of less than 10% and 1 case demonstrated an increase of between 10-20%.
- In the group with secondary dengue, out of 10

Table 1. Association Between Type of Dengue Infection With Gallbladder Edema

	Type of dengue infection		
	Primary	Secondary	Seronegative
Gallbladder edema	5	10	2
No gallbladder edema	15	8	17
	20	18	19

Chi square test $p=0,010$

cases with gallbladder edema, there were 5 cases with an increase in hematocrite level of over 20% and 5 cases with an increase of 10 to 20%.

- In the seronegative group, out of 2 cases with gallbladder edema, there was less than 10% increase in hematocrite level.

In the group without gallbladder edema, the percentage of increase of hematocrite level was as follows: 23 cases had an increase in hematocrite level of less than 10%, 14 cases of 10 to 20%, and 3 cases of less than 20%. Chi square did not reveal a significant association between gallbladder edema and elevation of hematocrite levels ($p=0.073$). Correlative analysis using the Spearman test found a weak yet significant association ($r_s=0.282$, $p=0.034$).

Table 2. Association Between Increased of Hematocrite Level With Gallbladder Edema

	Increased of hematocrite levels (%)		
	< 10	10-20	>20
Gallbladder edema	6	6	5
No gallbladder edema	23	14	3
	29	20	8

Chi square test $p=0,073$

Spearman test $\epsilon = 0,261$ $p=0,05$

DISCUSSION

DHF-associated hemoconcentration occurs due to plasma leakage from the vascular to the intracellular space due to inflammation and endothelial disorder. Plasma leakage occurs on the 4th to 7th day from the onset of fever and the fluid will be collected in interstitial spaces and serous cavities.^{4,5,6}

The fluid collects in serous cavities, such as the pleural and peritoneal cavities. The presence of clinical ascites is rarely reported by researchers possibly because the fluid collection is small. Nevertheless, ascites could be detected using ultrasound. Adult DHF patients are rarely found with pleural effusion and gallbladder wall edema. Gallbladder wall edema is often interpreted as cholecystitis.

Clinically, the abnormality is considered to play a role in the development of DHF-associated dyspepsia.^{3,7} The development of gallbladder edema in DHF generally does not change management policy, and the main treatment is still Ringer lactate or acetate infusion to suppress hemoconcentration, maintain blood circulation, and prevent shock. In this study, there is a tendency for a higher degree of hemoconcentration accompanied by an increased rate of gallbladder edema.

CONCLUSION

Based on this study, there was a significant association between the type of dengue infection and the development of gallbladder edema. The incidence of gallbladder edema was higher among the group with secondary dengue (55%) compared to those with primary dengue. There was a tendency (weak association) between elevated hematocrite levels and the development of gallbladder edema. The results of this study need to be supported by further studies with a prospective design and a larger number of dengue positive cases.

REFERENCES

1. Maria G. Guzman, Mayling Alvarez, et al. Fatal dengue hemorrhagic fever in Cuba, *J Infect Dis* 1997.
2. Gubler D, Clark G. Dengue/dengue hemorrhagic fever : the emergence of global health problem. *Emerg Infect Dis* 1995;1: 55-7.
3. Nimmannitya S. Management of dengue haemorrhagic fever. Monograph on dengue/dengue haemorrhagic fever. Regional publication SEARO No. 22. New Delhi : WHO Regional Office for South-East Asian;1993. p.48-54.
4. Sumarmo, Wulur H, Jahja E, Gubler DJ, Suharyono W, Soresen K. Clinical observations on virilogically confirmed fatal dengue infectious in Jakarta, Indonesia. *Bull WHO* 1983; 61: 693-701.
5. Nimmannitya S. Clinical spectrum and management of dengue haemorrhagic fever. *South-east Asian J Trop Med Pub Health* 1987; 392-7.
6. Halstead SB. Pathogenesis of dengue, challenges to molecular biology. *Science* 1988; 239: 475-81.
7. Iskandar Z. Dengue hemorrhagic fever and dyspepsia : correlation between platelet count and endoscopic findings. *Act Med Indones* 1995; 27: 163-70.