

Abdominal Disturbances among Dengue Fever Patients

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ABSTRACT

Background: Abdominal disturbances are common symptoms found in approximately 40% of patients with dengue fever, which frequently cause significant morbidity. This study was developed as an attempt to understand the effect of plasma leakage in dengue hemorrhagic fever; particularly on abdominal problems.

Method: The study was conducted in hospitalized patients who were diagnosed with dengue fever and dengue hemorrhagic fever (based on the 1997 WHO criteria for DHF) at Fatmawati hospital, Jakarta, Indonesia. Abdominal ultrasonography (USG) was done on the fourth to sixth day in every patient and when necessary, endoscopy was done. Data were analyzed by Chi-square test.

Results: Fifty-three (54.6%) patients had abdominal pain, 81 (83.5%) patients had nausea, 45 (46.4%) patients had excessive vomiting and 28 (28.9%) patients had diarrhea. Forty-seven (48.4%) patients had their aspartate aminotransferase (AST) elevated more than two fold of the Upper Normal Limit (UNL) level; 19 (20%) patients had their alanine aminotransferase (ALT) level elevated two fold higher than the UNL. Amylase was found to be two fold higher than the UNL only in 2 (2%) patients. Lipase level elevated two fold higher than the UNL in 11 (11.3%) patients. USG imaging showed that thickening of the gallbladder wall (over 3 mm) were observed in 83 (85.6%) patients. Endoscopic procedures showed erosive features particularly in the antrum, including edema of the gastric mucosa and widening of the gastric mucosa folding in four patients, while 4 (4.12%) patients had melena.

Conclusion: Abdominal disturbances such as abdominal pain, vomiting, melena, liver enlargement and abnormal liver function as well as thickening of the gallbladder wall more than five mm are significantly high in patients with dengue hemorrhagic fever.

Keywords: abdominal disturbances, plasma leakage, dengue hemorrhagic fever

INTRODUCTION

Indonesia is an endemic country for dengue fever. Clinical manifestation or symptoms that experienced by the patients are caused not only by the direct effect of the virus but also by the acute increment of vascular permeability, which may lead to plasma

leakage into extravascular space. Coagulation and thrombocytopenia could also implicate symptoms to the patients.

Symptoms found in patients with dengue fever other than fever, headache, cramps, retroorbital pain include abdominal pain, nausea, vomiting, and diarrhea. Approximately 40% of dengue fever patients suffer from abdominal disturbances. Many prior studies have demonstrated that the causes of abdominal disturbances in dengue fever patients are as follows: acute hepatitis, acute cholecystitis, acute appendicitis, acute enteritis, and erosive gastritis.

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This study was developed as an attempt to understand about how powerful is the impact of dengue fever and plasma leakage in dengue hemorrhagic fever to produce the aforementioned abdominal disturbances such as abdominal pain, nausea, vomiting, diarrhea, and disruption of abdominal organs including the liver, pancreas, gall bladder and upper gastrointestinal tract.

METHOD

All patients who were newly diagnosed with dengue fever and dengue hemorrhagic fever and had been hospitalized at Fatmawati hospital since March 15th, 2009 until the desired number of patients has been achieved were included in this study. The number of samples was calculated by single proportion estimation formula. By having statistical assumption for confidential degrees of 95% (1- α), incidence proportion of 40%, and precision of 10%, finally the number of minimal sample were decided as 93 samples.

Diagnosis of dengue fever and dengue hemorrhagic fever were established based on WHO 1997 criteria for DHF. The patients whom diagnosis had been established underwent laboratory studies, i.e. aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, direct and indirect bilirubin, albumin, APTT, PT, amylase, lipase; while the IgM/IgG anti-dengue tests were taken seven days after the onset by using Oncoprobe rapid-strip-tests, which is a qualitative scoring. Abdominal USG were performed within the 4-6 days after the onset of illness by radiologist using Toshiba Just Vision 400. Those tests were performed to detect any abnormalities in liver, spleen, pancreas, gall bladder, kidney; including ascites and pleural effusion. In addition, endoscopic examinations were performed in patients who were suffering hematemesis or melena. All laboratory studies, USG and endoscopic examinations were performed at Fatmawati Hospital.

Data were analyzed by using statistical SPSS 16 and Chi-square test, where $p < 0.05$ was considered to significant difference.

RESULT

We found 97 patients who met the 1997 WHO criteria for DHF, of whom were 53 (54.6%) patients with dengue fever and 44 (45.4%) patients with dengue hemorrhagic fever. Based on sex, we found 53 (54.6%) male patients and 44 (45.4%) female patients; 28 patients were under 20 years old, 63 patients were between 20-50 years old, and 6 patients were above 50 years old; 38 patients were underweight, 41 patients were ideal body weight, and 15 patients were overweight. Dengue fever patients

occurred more frequent in younger ages. Such difference was statistically significant as shown by Chi-square test ($p < 0.05$)

Based on history taking during hospital admission, all patients had history of fever; however, 44 patients had never got fever since the admission day until they were discharged. We found headache in 75 (77%) patients; retroorbital pain in 30 (31%) patients, muscle pain in 75 (77%) patients, gum bleeding in 9 (9%) patients and epistaxis in 4 (4%) patients. By physical examination, we found petechiae in 58 (60%) patients, positive Rumpel-Leede tests were found in 77 (79%) patients, hepatomegaly were found in 22 (23%) patients and splenomegaly was not found.

The laboratory study demonstrated leukopenia in all patients, i.e. less than 2,000/ μ L in 20 (21%) patients, 2,000-3,000/ μ L in 66 (68%) patients and 3,000-5,000/ μ L in 11 (11%) patients. Thrombocytopenia was found in all patients, including less than 10,000/ μ L in 15 (15%) patients, 10,000-50,000/ μ L in 46 (47%) patients and 50,000-100,000/ μ L in 36 (37%) patients. Positive results of IgM anti-dengue fever test were found in 27 (35.1%) dengue fever patients and 18 (23.4%) dengue hemorrhagic fever and IgG anti-dengue were found positive in 31 (40.3%) patients with dengue fever and 24 (31.2%) patients with dengue hemorrhagic fever (table 1).

By using Chi-square analysis, we found statistically significant difference on the severity of thrombocytopenia between dengue fever and dengue hemorrhagic fever patients. Severe thrombocytopenia were found more frequently in dengue hemorrhagic fever patients than in dengue fever patients.

Based on history taking during hospital admission, several abdominal disturbances were found, 53 (55%) patients had abdominal pain, 81 (84%) patients had nausea, 45 (46%) patients had vomiting, 28 (29%) patients had diarrhea; 1 (1.03%) patient had hematemesis and 4 (4.12%) patients had melena.

Epigastric pain, vomiting, and melena, were found more frequently in dengue hemorrhagic fever patients than in dengue fever patients. This difference was statistically significant as demonstrated by Chi-square analysis tests ($p < 0.05$).

The physical examination in abdominal area revealed hepatomegaly in 22 (22.68%) patients, abdominal tenderness in 57 (58.76%) patients; while splenomegaly was not found. Abdominal tenderness was found more frequently in dengue hemorrhagic fever patients than in dengue fever. Such difference was statistically significant as shown by Chi-square analysis test ($p < 0.05$). In contrast, other physical examinations such as hepatomegaly, splenomegaly, and defans muscular were not statistically significant in both groups.

Table 1. Characteristics of dengue fever and dengue hemorrhagic fever patients

Characteristic	Dengue fever n (%)	Dengue hemorrhagic fever n (%)	Total	p
Sex				
Male	29 (29.9)	24 (24.7)	53	0.98
Female	24 (24.7)	20 (20.7)	54	
Age (year)				
< 20	9	19	28	0.01
20-50	39	24	63	
> 50	5	1	6	
Body weight (kg)				
Underweight	16	22	38	0.08
Ideal	25	16	41	
Overweight	11	4	15	
Fever				
No fever	23 (23.7)	21 (21.6)	44	0.74
1-2 days	26 (26.8)	21 (21.6)	47	
> 3 days	4 (4.1)	2 (2.1)	6	
Headache	40 (41.2)	35 (36.1)	75	0.63
Retroorbital pain	16 (16.5)	14 (14.4)	30	0.86
Cramps	40 (41.2)	35 (36.1)	75	0.63
Gum bleeding	5 (5.1)	4 (4.1)	9	1
Epistaxis	2 (2.1)	2 (2.1)	4	1
Petechi	30 (30.9)	28 (28.9)	58	0.48
Positive RL test	39 (40.2)	38 (39.2)	77	0.12
Leukocytes (/ μ L)				
< 2,000	10 (10.3)	10 (10.3)	20	0.33
2,000-3,000	39 (40.2)	27 (27.8)	66	
> 3,000	4 (4.1)	7 (7.2)	11	
Platelets (/ μ L)				
< 10,000	2 (2.1)	13 (13.4)	15	< 0.0001
10,000-50,000	21 (21.6)	25 (25.8)	46	
> 50,000	30 (30.9)	6 (6.2)	36	
Lymphocytes (/ μ L)				
< 40	21 (21.6)	15 (15.5)	36	0.39
\geq 40	25 (25.8)	26 (26.8)	51	

Table 2. Disturbances, examination and USG results of abdomen in dengue fever and dengue hemorrhagic fever patients

	Dengue fever n (%)	Dengue hemorrhagic fever n (%)	Total	p
Abdominal disturbances				
Epigastric pain	24 (24.7)	29 (29.9)	53	0.042
Nausea	44 (45.4)	37 (38.1)	81	0.88
Vomiting	18 (18.6)	27 (27.8)	45	0.007
Diarrhea	14 (14.4)	14 (14.4)	28	0.55
Hematemesis	1 (1.03)	0 (0)	1	1
Melena	0 (0)	4 (4.1)	4	0.039
Abdominal examination				
Hepatomegaly	10 (10.3)	12 (12.4)	22	0.32
Splenomegaly	-	-	-	
Abdominal tenderness	24 (24.7)	33 (34.0)	57	0.003
Rebound pain	3 (3.1)	3 (3.1)	6	1
Defens muscular	1 (1.0)	2 (2.1)	3	0.58
USG result				
Hepatomegaly	15 (15.5)	22 (22.7)	37	0.034
Splenomegaly	13 (13.4)	17 (17.53)	30	0.15
Acute pancreatitis	1 (1.0)	0	1	1
Gallbladder wall thickening > 5 mm	20 (20.6)	34 (35.1)	54	< 0.0001

Laboratory study suggested statistically significant results of AST and ALT level between the dengue fever group and dengue hemorrhagic fever group. AST and ALT test results were more than 2 fold above the upper normal limit, and it occurred more frequently in dengue hemorrhagic fever patients. On the contrary, the test results of amylase, lipase, alkaline phosphatase, and bilirubin demonstrated no statistically significant difference between both groups.

Based on abdominal USG, we found hepatomegaly

in 22 patients from the dengue hemorrhagic fever group and 15 patients from the dengue fever group. Splenomegaly were found in 17 patients with dengue hemorrhagic fever and 12 patients with dengue fever; pancreatic disorder was not found in both groups; thickening gallbladder walls more than 5 mm were found in 34 patients with dengue hemorrhagic fever and 20 patients with dengue fever. We found a statistically significant difference in gallbladder wall thickening among both groups.

Table 3. Laboratory examination of liver and pancreas function in dengue fever and dengue haemorrhagic fever patients

	Dengue fever n (%)	Dengue hemorrhagic fever n (%)	Total	p
Amylase (μL)				
< 53	35 (36.1)	30 (30.9)	65	0.25
53–106	15 (15.5)	10 (10.3)	25	
> 106	0	2 (2.1)	2	
Lipase (μL)				
< 46	19 (19.6)	22 (22.7)	41	0.15
46–92	26 (26.8)	13 (13.4)	39	
> 92	5 (5.1)	6 (6.2)	11	
AST (IU/L)				
< 35	12 (12.4)	6 (6.2)	18	0.001
35–70	19 (19.6)	2 (2.1)	21	
> 70	21 (21.6)	26 (26.8)	47	
ALT (IU/L)				
< 40	27 (27.8)	8 (8.2)	35	0.001
40–80	19 (19.6)	16 (16.5)	35	
> 80	5 (5.1)	14 (14.4)	19	
Albumin (g/dL)				
< 3.5	16 (16.5)	20 (20.6)	36	0.16
\geq 3.5	27 (27.8)	18 (19.78)	45	
Bilirubin (mg/dL)				
< 1	40 (41.2)	32 (33.0)	72	0.10
\geq 1	4 (4.1)	9 (9.3)	13	

Table 4. Ascites and pleural effusion in patients with dengue fever based on hemoconcentration

	Hemoconcentration			p
	< 10%	10–20%	> 20%	
	n (%) = 21 (22.3)	n (%) = 49 (52.1)	n (%) = 24 (25.5)	
Ascites	2 (2.1)	12 (12.8)	13 (13.8)	0.003
Pleural effusion	3 (3.1)	6 (6.4)	13 (13.8)	< 0.0001

Although hemoconcentration was still less than 20%, ascites was found in 13 (13.5%) patients of the dengue fever group and 15 (15.6%) patients of the dengue hemorrhagic fever group; pleural effusion was found in 13 (13.5%) patients of the dengue fever group and 11 (11.5%) patients of the dengue hemorrhagic fever group.

There were 4 patients with melena and all of them were from the dengue- hemorrhagic fever group. Only two patients were willing to have endoscopic examination. We found erosive mucosa especially in antrum area, widened mucosal folds and edema of gastric mucosa.

DISCUSSION

Abdominal disturbances such as epigastric pain, nausea, vomiting, and diarrhea are complaints that frequently found in dengue hemorrhagic fever patients. Those complaints are so annoying that may lead patients for hospital visit. In this study, such complaints including epigastric pain, nausea, vomiting, and melena were found more frequently in the dengue hemorrhagic fever group compared to dengue fever. Through statistical analysis tests, such difference was considered statistically significant ($p < 0.05$). The result is not different from prior studies.^{1,3}

Several previous studies had already correlated the abnormality of intraabdominal organs (liver, pancreas, and spleen) as the causes of abdominal

disturbances. Such abnormality includes several diseases, i.e. acute hepatitis, acute pancreatitis, cholecystitis, acute appendicitis, and acute enteritis. In this study, a number of abnormalities had been found, they were acute hepatitis, cholecystitis, acute pancreatitis, erosive gastritis, and acute enteritis.³

The manifestation of acute hepatitis in dengue fever and dengue haemorrhagic fever patients could be recognized based on symptoms, physical examination, laboratory tests and abdominal USG. In this study, abdominal pain occurred in 53 (55%) patients, nausea in 81 (84%) patients, vomiting in 45 (46%) patients and fever preceded in all patients, we may also conclude those complaints as the classic prodromal symptoms of acute hepatitis. The physical examinations revealed abdominal tenderness in 57 (59%) patients, palpable hepatomegaly in 22 (23%) patients, which was increased to 37 (38%) patients by abdominal ultrasound. Based on laboratory tests, we found 21 (22%) patients with elevated AST level less than two fold of the upper normal limit (UNL); while elevation more than two fold of the upper normal limit were found in 47 (48%) patients and 35 patients had their ALT level less than two fold of the UNL, while two fold higher than the UNL were found in 19 (20%) patients. Some scientists have previously suggested such liver abnormality as reactive hepatitis.^{4,5,6}

Complaints of abdominal pain, nausea, hepatomegaly, and elevated AST and ALT level occur more frequently in patients with dengue hemorrhagic fever than patients with dengue fever. Using Chi-square analysis, the difference was statistically significant ($p < 0.05$). This finding was not different from prior studies.^{4,5,6} Although liver is not the target organ of dengue fever, pathological evidences had been found of patients who died from Dengue Shock Syndrome, such as centrilobular necrosis, fatty changes, kupfer cell hyperplasia, acidophilic bodies and monocytes infiltration in portal area.¹

In addition to the symptoms of abdominal pain, nausea, vomiting, and abdominal tenderness, the evidence of gall bladder disorders can be recognized by abdominal USG. There were 83 (85.6%) patients who had thickened gallbladder wall more than 3 mm that we considered as upper normal limit of gallbladder wall and the occurrence of non-calculus acute cholecystitis. In this study, we found 54 (56%) patients had their gallbladder wall thicker than 5 mm. Thirty-four (35%) patients with dengue hemorrhagic fever had their gallbladder wall thicker than 5 mm, while for dengue fever group, there were 20 (21%) patients. Such findings were statistically significant as shown by Chi-square analysis ($p < 0.05$). In pediatric patients, gallbladder wall thickening was found more frequently, i.e. up to 100% of patients.⁷ Wu et al, found that 59% of gallbladder wall thickening occur in adult dengue fever patients.⁸

In this study, we didn't find any pancreas disorder by abdominal USG. This was almost similar with the previous study, in which pancreas disorder was not found in any of dengue fever and dengue hemorrhagic fever patients.⁹

Laboratory findings of amylase and lipase showed significant elevated level. The amylase level elevated less than two fold above the upper normal limit in 25 (26%) patients, while more than two fold elevation above the upper normal limit were found in 2 (2%) patients. In addition, there were 25 (26%) patients had their lipase level elevated less than two-fold above the upper normal limit; while 11 (11%) patients had their lipase level elevated more than two-fold above the upper normal limit. Although the number of patients in the dengue fever group and in dengue hemorrhagic-group was different, but such difference was not statistically significant as demonstrated by Chi-square analysis test.

Melena occurred in four patients and all of them were from the dengue- hemorrhagic fever group. Only two of them were willing to have endoscopic examination. Based on the endoscopic examination, we found erosive mucosa of antrum part of gaster, mucosa

edema, and widened gastric fold. Abnormality that most frequently found on endoscopic examination of dengue hemorrhagic fever patients who experienced gastrointestinal bleeding is erosive gastritis.^{10,11}

CONCLUSION

Dengue fever and dengue hemorrhagic fever may cause abdominal disturbances such as nausea, epigastric pain, vomiting, and diarrhea. Common causes include acute hepatitis, acute non-calculi cholecystitis, acute pancreatitis, and erosive gastritis.

Abdominal disturbances are significantly more common in patients with dengue hemorrhagic fever than dengue fever. We can conclude that plasma leakage is playing more important role in producing symptoms and disorder we found in those patients.

We need further research and suggestions of the more rational treatment for abdominal disturbances that appropriate to the pathogenesis of such disturbances, including proton pump inhibitor treatment that commonly given in daily practices to overcome those symptoms.

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