Cardiovascular change in children with dengue shock syndrome

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Abstract. To determine the cardiovascular changes in children with dengue shock syndrome. Echocardiography was performed in 8 children (5 females) with dengue shock syndrome, median age 6.5, 4.2–13.7 yr and weight 34, 12–66 kg. All had massive bleeding with low initial hematocrit in most cases (median 31%), thrombocytopenia (median platelet 37,000/μL), and coagulopathy with massive pleural effusion. Seven (87.5%) developed acute renal failure and hepatic failure. All patients were in either compensate or decompensate shock with alteration of consciousness, tachycardia, poor tissue perfusion, and prolonged capillary refill (>4 s) with mean arterial pressure 65, 39–94 mm Hg. The cardiac dimension was normal to low normal except one had dilated left ventricle. Seven patients had normal left ventricular systolic function (5 with inotrope infusion). One patient had impaired systolic function even with inotrope. All had normal cardiac index (4.14, 3.51–6.37 L/min/m^2) with increased heart rate (141.5, 110–160/min) but low stroke volume index (30.72, 25.37–42.49 mL/m^2) and low systemic vascular resistance index (1,072, 223–2,880 dyne/sec/cm^{-5}/m^2). Decreased preload from bleeding and vascular leakage into the third space play an important role in shock in Dengue. However, decreased stroke volume and low systemic vascular resistance may be additional causes of shock.

Keywords: Dengue hemorrhagic fever, echocardiography, shock, hemodynamic, hemorrhage, pediatrics

1. Introduction

Dengue virus infection is quite common in children especially in tropical countries [1]. It has a wide spectrum of manifestations including dengue fever, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). DSS defined as DHF grade 3 or 4 which has shock is the most serious condition [2]. The mortality in case with DSS can be as high as 44% [3].

The pathogenesis of DSS is not well understood. In the past, hemodynamic studies in 5 patients with DHF in which 4 were in clinical shock and 1 was in impending shock demonstrated reduced cardiac output and increased peripheral resistance in all patients, indicating that shock was due to decreased cardiac output rather than to arteriolar dilatation [4]. Two mechanisms explaining low cardiac output were hypovolemia and venous pooling [5]. Kapra reported decreased ejection fraction (EF) by modified Simpson (< 50%) in 9 of 54 (16.7%) children with dengue fever, DHF, and DSS in which 2 of 9 had significant decrease (EF < 35%). However, the 9 children were in all stages of clinical severity [4]. Other studies have

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also reported left ventricular systolic dysfunction in adult patients and in children with DHF [6–9]. However, there were no DHF grade 4 cases in those studies. The role of myocardial function in patients with DHF and DSS is still unclear, especially in those who have shock. The aim of the present study was to evaluate the cardiac function and other hemodynamic parameters including systemic vascular resistance (SVR), systemic vascular resistant index (SVRI), stroke volume (SV), stroke volume index (SVI), cardiac output (CO), and cardiac index (CI) in children with DSS grade 4.

2. Methods

2.1. Study population

Eight patients with DSS grade 4 admitted to pediatric intensive care unit (PICU) at the University tertiary Hospital from year 2006 to 2009; were enrolled in the study. The WHO definition of DHF and DSS included fever; hemorrhagic manifestations; thrombocytopenia ($\leq$100,000/μL); evidence of plasma leakage due to increased vascular permeability including hemoconcentration, hematocrit (Hct) increased by 20% or more, a drop in Hct following volume-replacement treatment $\geq$20% of baseline, or objective evidence of increased capillary permeability such as pleural effusion, ascites, and hypoproteinaemia; and evidence of circulatory failure such as rapid and weak pulse, narrow pulse pressure (<20 mmHg), hypotension for age (this is defined as systolic pressure <80 mmHg for those less than five years of age, or <90 mmHg for those five years of age and older), or cold clammy skin and restlessness [9]. All patients were subjected to clinical evaluation, laboratory investigation, chest film, and echocardiography. A revised pediatric index of mortality (PIM2), which estimates mortality risk from data readily available at the time of ICU admission [10] and pediatric risk of mortality III (PRISM III), which is the third-generation pediatric physiology-based score for mortality risk [11] were calculated from the data of all patients.

This study was approved by committee on human rights related to researches involving human subjects, Faculty of Medicine, Ramathibodi Hospital, Mahidol University.

2.2. Confirmation of dengue virus infection

The dengue specific IgM and IgG antibody were determined by capture ELISA technique in all patients.

Positive result was expressed by the ratio of the optical density reading of the sample and controlled serum $\geq$1. Dengue virus infection was defined as primary infection when the ratio of dengue-specific IgM to IgG$\geq$1.8:1 whereas secondary infection was defined as ratio of <1.8:1 [12]. Reverse transcriptase-polymerase chain reaction (RT-PCR) was carried out using serotype-specific primers in the seminested polymerase chain reaction as described [13].

2.3. Echocardiography study

Echocardiography was performed in all children within the first hour after admission in PICU, using Hewlett Packard Sonos 4500. LV dimensions including left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD) were measured by M-mode using parasternal short axis view at the level of papillary muscles. Cardiovascular parameters were calculated (Table 1).

2.4. Statistical analysis

Descriptive analysis was used with all continuous variables expressed as the median and range.

3. Results

Eight patients, 5 females, median age of 6.5 (4.2–13.7 years), weight of 34 (12–66 kg.), and body surface area (BSA) of 1.1 (0.5–1.7 m^2) were referred from the rural hospital after fluid resuscitation to our PICU. All were diagnosed as secondary dengue virus infection proved by serologic assay with DSS grade 4. Four patients were referred after 1 day of leakage state and other 4 patients on day of leakage. However, 6 patients still had fever on day of admission. Active bleeding was found in 7 of 8 patients (87.5%) including upper and/or lower gastro-intestinal (GI) bleeding, endotracheal tube bleeding (n = 6), site of cut down (n = 1), and hypermenorrhea (n = 1). Seven of 8 patients had endotracheal tube insertion before or right after admission with ventilator support due to respiratory failure while the remaining one (patient 1) was intubated 10 hr after admission. All had massive pleural effusion (bilateral, n = 5; and right, n = 3) requiring bilateral intercostals drainage (ICD) in 2 and right ICD in 1 patient. Five had minimal pericardial effusion. The predicted mortality

Table 1
Methods of calculations in cardiovascular parameter

Parameters	Units	Calculation	Normal values	
			Male	Female
LVEDV	mL	[a][7/(2.4+LVEDD)].[LVEDD]^3	-	
LVESV	mL	[a][7/(2.4+LVESD)].[LVESD]^3	-	
LVEDVI	mL/m^2	LVEDV/BSA	[b]62–120	[b]58–103
LVEF	%	[a](LVEDV-LVESV)/LVEDV	[c]≥55	
LVFS	%	[a](LVEDD-LVESD)/LVEDD	[c]≥25	
P_LVEDD	%	[45.3*BSA^3]–[0.03*age] − 7.2	-	
%LVEDD	%	[d](LVEDD/P_LVEDD)*100	[c]<112	
SV	mL	LVEDV-LVESV	-	
SVI	mL/m^2	SV/BSA	[e]40–85	
CO	L/min	SV*HR	-	
CI	L/min/m^2	CO/BSA	[e]≥2.5	
SVRI	dynes/sec/cm^{-5}/m^2	(MAP-CVP)/CI	[e]1,970–2,390	

BSA: body surface area; CI: cardiac index; CO: cardiac output; left ventricular end-diastolic dimension: LVEDD, LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; LVESD, left ventricular end-systolic dimension; LVESV, left ventricular end-systolic volume; mL, milliliter; m^2, square meter; P_, predicted; SV, stroke volume; SVI, stroke volume index; SVRI, systemic vascular resistance index; %LVED, the ratio of LVEDD to predicted LVEDD expressed in percentage.

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[e]Normal lab values. Available from URL: www.mtworld.com/tools_resources/labvalues.html/ Accessed Apr 21, 2010.

by PRISM-III and PIM scores were high with median PRISM-III of 16.5 [10–19] and PIM predicted mortality of 13.6 (3.8–57.5%). Table 2 summarized clinical characteristics in each patient.

Initial laboratory findings were as following. The median hematocrit (Hct) was 31 (22–56%). Only two patients had hemoconcentration (Hct 56% and 43%). Thrombocytopenia and coagulopathy were present in all. Five patients (62.5%) had elevated creatinine (Cr) and blood urea nitrogen (BUN), however, 7 patients eventually developed acute renal failure (ARF) defined as a rising of creatinine. All had elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyltransferase (GGT). Only one had slightly elevated ALT (54 U/L) and elevated AST (254 U/L) while the others had moderate to severe elevation of which 7 developed acute hepatic failure and 6 developed hepatic encephalopathy in their clinical courses. Seven patients (87.5%) had hypoalbuminemia (<35 g/L). Severe metabolic acidosis (base excess >-10) was found in 5 of 8 patients with median base excess of −11.4 ([−21.3] – [8.8]) and median pH 7.29 (7.04–7.55). The coagulogram was abnormal in all patients. Table 3 summarized initial laboratory findings in each patient.

Hemodynamic assessment including blood pressure (BP), heart rate (HR), central venous pressure (CVP), and echocardiography were performed within one hour of admission at the PICU. All patients were in shock state with alteration of consciousness, tachycardia, poor tissue perfusion, and prolonged capillary refill (>4 s) either compensate shock (normal BP) or decompensate shock (low BP) with median of mean arterial pressure (MAP) of 65 (39–94 mmHg). Initial CVP were high (recorded in 5 patients), however the ratio of left ventricular end-diastolic dimension (LVEDD) to predicted LVEDD expressed in percentage (%LVEDD) was normal to low normal, median 89.19 (81.91–116.20%) except one (patient 4) who had %LVEDD equal to 116% (normal < 112%). HR was increased in all patients, median 141.5 (110–160/min). Most (6 of 8 patients) had left ventricular end-diastolic volume index (LVEDVI) lower than normal, median 46.97 (37.46–90.64 mL/m^2) and the other two had normal LVEDVI. Seven patients had normal left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS), however, 5 of 7 patients had inotrope infusion including dobutamine and/or dopamine while performing echocardiography. One patient (patient 4) had impaired left ventricular systolic function (LVEF 47% and LVFS 23%) even with

Table 2
Patients' characteristics and their clinical manifestations, clinical courses, complications, and clinical outcomes

Patient characteristics and clinical	Pt.1	Pt.2	Pt.3	Pt.4	Pt.5	Pt.6	Pt.7	Pt.8	Median (range)
Age (years)	6.4	8.4	5.1	4.2	13.7	4.8	6.6	12.3	6.5 (4.2–13.7)
Sex	F	M	F	M	M	F	F	F	-
Bleeding	UGI	U+L GI, IA,	U+L GI	UGI	U+L GI	U+L GI	ETT,	U+L GI	-
	NA	Active	Active	IA, Active	Active	Active	cutdown wound Active	Hypermen Active	-
Temp (°C)	40.2	38.5	39	38.3	38	37.2	40.2	37.0	38.4 (37.0–40.2)
Day after onset of fever	6	7	4	5	4	6	5	8	5.5 (4–8)
Pleural effusion	Ma, R	Ma, B	Ma, B	Ma, B	Ma, R	Ma, R	Ma, B	Ma, B	-
Pericardial eff	Min	Min	Min	No	Min	Min	No	No	-
CT ratio	0.51#	0.43	0.44	0.47	0.44	0.43	0.49	0.51#	-
PRISM-III	10	12	16	11	19	17	17	19	16.5 (10–19)
PIM-II (% of death)	3.8	13.5	13.6	10.3	57.5	20.8	11.4	34.6	13.6 (3.8–57.5)
ICD	-	B	B	R	-	-	-	-	-
Dialysis	-	PD, CVVH	PD, HD, CVVH	PD	PD, CVVH	CVVH	PD, CVVH	CVVH	-
Central line	-	LFV	RFV	RSV	RFV	LFV	RFV	RFV	-
Hep fail/encep	No/no	P/P	P/P	P/no	P/P	P/P	P/P	P/P	-
ARF	No	P	P	P	P	P	P	P	-
Coagulopathy	P	P	P	P	P	P	P	P	-
Inotropes/vasopressors	DP	Epi, *DP	*DB, DP	*DB, E, NE	E, DP, DB	*DB, *DP, *NE	E, *DP, DB,NE	E, DP, NE, DB	-
LOS (Days)	5	13	10	3	9	6	44	3	7.5 (3–44)
Outcome	Alive	Dead	Dead	Dead	Dead	Dead	Alive	Dead	-
Other complications	None	HP ARDS VAP	Sepsis Septic shock Brain death	AFI PHT ARDS VAP LCOS	Sepsis ARDS IAP MAT Severe brain edema	Severe brain swelling (CT) Brain death	Pulm candidiasis ARDS IAHS Pressure sore	Intractable metabolic acidosis, Unstable BP	-

AFL: atrial flutter; ARDS: adult respiratory distress; ARF: acute renal failure; B: bilateral; BP: blood pressure; CVVH: continuous veno-venous hemofiltration; DB: dobutamine; DP: dopamine; E: epinephrine; eff: effusion; ETT: endotracheal tube; F: female; GI: gastrointestinal; HD: hemodialysis; HP: hemoperitoneum; IA: intraabdominal; IAHS: infectious associated hemophagocytic system; IAP: invasive aspergillosis pneumonia; ICD: intercostal drainage; L: lower; LCOS: low cardiac output state; LFV: left femoral vein; LOS: length of stay; M: male; Ma: massive; Min: minimal; MAT: multifocal atrial tachycardia; NA: non-active; NE: norepinephrine; P: present; PD: peritoneal dialysis; PHT: pulmonary hypertension; PIM-II: pediatric index of mortality II; PRISM-III: pediatric risk of mortality III; Pt: patient; Pulm: pulmonary; R: right; RFV: right femoral vein; RSV: right subclavian vein; VAP: ventilator associated pnuemonia; #: not full inspired chest film; *started at the time of admission.

Table 3
Initial laboratory findings

Lab.	Pt.1	Pt.2	Pt.3	Pt.4	Pt.5	Pt.6	Pt.7	Pt.8	Median (range)
WBC (/μL)	4,280	14,500	4,030	5,650	10,900	9,260	9,430	12,380	9,345 (4,030–14,500)
Hct (%)	43	34	56	26	30	24	22	31	31 (22–56)
Platelet (/μL)	35,000	34,000	53,000	39,000	29,000	23,000	60,000	51,000	37,000 (23,000–60,000)
Na (mmol/L)	139	134	136	138	139	136	140	137	138 (134–140)
K (mmol/L)	5.2	4.3	3.9	3.3	6.3	5	3.8	6.4	4.7 (3.3–6.4)
CO_2 (mmol/L)	28.4	9.9	22.3	24.4	4.9	9.7	14.6	5.9	12.3 (4.9–28.4)
AST (U/L)	394	16,003	1,297	265	9,560	17,024	5,136	13,494	7,348 (265–17,024)
ALT (U/L)	189	2,948	346	54	3,456	4,237	865	3,299	1,907 (54–4,237)
GGT (U/L)	107	159	452	23	191	39	59	121	114 (23–452)
TP (g/L)	66.5	48.5	64.4	43	28.5	46.3	33.1	47.4	46.9 (28.5–66.5)
Alb (g/L)	36.3	26.9	30.5	23.2	11.4	24.6	13.5	16.6	23.6 (11.4–36.3)
BUN (mg/dL)	12.9	30.8	13.2	9.8	15.7	53.2	14.3	40	15 (9.8–53.2)
Cr (mg/dL)	0.3	1.3	0.5	0.7	2.2	2.4	1.4	3.7	1.4 (0.3–3.7)
pH	7.55	7.27	7.14	7.34	7.04	7.45	7.30	7.09	7.29 (7.04–7.55)
PCO_2 (mmHg)	34.8	21.1	80.9	53.5	26	14.9	26.1	28.9	27.5 (14.9–80.9)
PO_2 (mmHg)	85.4	189.8	95.4	90.8	64.8	332.7	89.2	77.7	90 (64.8–332.7)
BE (mmol/L)	8.8	−14.7	−3.8	3.5	−21.3	−11.3	−11.4	−19.2	−11.4 [(−21.3)–(8.8)]
PTT (sec)	44.6	101.9	50.5	46.8	200	82.5	200	200	92.2 (44.6–200)
PT (sec)	7.4	37.6	10.5	14.5	200	37	30.8	27.2	29 (7.4–200)
TT (sec)	37.6	25.4	13	13.2	21.7	21.8	22.3	13.7	17.7 (11.6–25.4)

Alb: albumin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BE: base excess; BUN: blood urea nitrogen; CO_2: carbondioxide content; Cr: creatinine; GGT: gamma-glutamyltransferase; Hct: hematocrit; K: potassium; Na: sodium; PCO_2: partial carbondioxide; PO_2: partial oxygen; PT: prothrombin time; PTT: partial prothrombin time; TP: total protein; TT: thrombin time; WBC: white blood count.

Table 4
Initial hemodynamic parameters

Parameters	Pt.1	Pt.2	Pt.3	Pt.4	Pt.5	Pt.6	Pt.7	Pt.8	Median (range)
BSA (m^2)	1.56	0.89	0.76	0.50	1.99	0.58	1.34	1.85	1.11 (0.50–1.99)
HR (/min)	140	143	140	150	145	140	160	110	141.5 (110–160)
LVEDDI (cm/m^2)	2.38	4.30	3.97	6.66	2.21	4.70	2.60	2.38	3.29 (2.21–6.66)
LVEDD% (%)	82.30	105.58	88.58	116.20	89.28	89.10	81.91	91.88	89.19 (81.91–116.20)
LVEDVI (mL/m^2)	37.47	70.30	46.58	90.64	43.96	47.33	37.46	47.49	46.97 (37.46–90.64)
LVEF (%)	74	57	67	47	60	64	68	67	65 (47–74)
LVFS (%)	42	29	36	23	30	33	37	37	36 (23–42)
SVI (mL/m^2)	27.79	40.11	31.24	42.49	26.42	30.21	25.36	31.91	30.72 (25.37–42.49)
CI (L/min/m^2)	3.89	5.74	4.37	6.37	3.83	4.23	4.06	3.51	4.14 (3.51–6.37)
CVP (mmHg)	-	15	14	12	-	15	19	-	15 (12–19)
SBP (mmHg)	113	108	127	81	67	68	54	80	81 (54–127)
DBP (mmHg)	50	85	78	64	44	38	32	50	57 (32–85)
MAP (mmHg)	91	93	94	70	52	48	39	60	65 (39–94)
SVRI (Dynes/sec/cm^{-5}/m^2)	768	1,377	2,561	2,880	271	1,881	223	401	1,072 (223–2,880)

BSA, body surface area; CI, cardiac index; CVP, central venous pressure; DBP, diastolic blood pressure; HR, heart rate; LVEDDI, left ventricular end-diastolic dimension index; LVEDD%, percentage of LVEDD to predicted LVEDD; LVEF, left ventricular ejection fraction; LVFS, left ventricular shortening; MAP, mean arterial pressure; SBP, systolic blood pressure; SVI, stroke volume index; SVRI, systemic vascular resistance index.

inotrope. All had normal CI, median of 4.14 (3.51–6.37 L/min/m^2) but most (6 of 8 patients) had low SVI, median 30.72 (25.37–42.49 mL/m^2) and most (6 of 8 patients) had low SVRI, median 1,072 (223–2,880 dyne/sec/cm^{-5}/m^2). Table 4 summarized hemodynamic parameters in each patient.

During their courses in the PICU, all patients with DSS were treated by fluid resuscitation either with colloid and isotonic solution and urgent transfusion of blood components especially packed red cells and platelets as needed. Five of 8 patients were started with inotropes either dobutamine and/or dopamine. Subsequently, all patients received inotrope/vasopressors to support their circulation. Seven of 8 (87.5%) had ARF and hepatic failure while only one patient (patient 1) did not have both. ARF was treated by peritoneal

dialysis, hemodialysis, and/or continuous veno-venous hemofiltration (CVVH). Six of 7 with hepatic failure also had hepatic encephalopathy. Median length of stay was 7.5 (3–44 days). The shock state was resolved with stable vital signs and hemodynamics in 7 of 8 patients during the first few days. One patient (patient 8) had unstable BP with intractable metabolic acidosis even after adequate fluid replacement and high dose of inotrope and vasopressors. This patient was in coma with fixed dilated pupils and also developed multifocal atrial tachycardia. He deteriorated with low BP and died 3 days after admission. One patient (patient 4) had stable vital signs after treatment. He had ventricular septal defect (VSD) and underwent surgical repair with patch closure of the VSD at other hospital 6 months before this admission. Initially, he was the only patient who had low LVEF (46%) and his LVEF improved after inotrope infusion. He had progressive pneumonia with adult respiratory distress syndrome (ARDS), but his vital signs could be maintained. On day 3 of admission, he developed atrial flutter with unstable BP requiring successful direct current cardioversion and also low cardiac output state (LCOS) with unstable vital signs. Echocardiography revealed deterioration of the ejection fraction and moderate tricuspid regurgitation (TR) with elevated estimated right ventricular systolic pressure by Doppler gradient of TR, indicating severe pulmonary hypertension (75% of systemic BP). His BP could not be maintained and he died 3 days after admission. The other 4 patients (patients 2, 3, 5, and 6) had stable vital signs after the first few days but had complications. Two patients (patients 3 and 5) had superimposed infection, unstable vital signs, and severe brain edema and died 10 and 9 days after admission. One patient (patient 2) with ventilator associated pneumonia (VAP) and ARDS died 13 days after admission; and one patient (patient 6) with severe brain edema and brain death died 9 days after admission. Overall, the mortality rate was 75%. Two patients (patient 1 and 7) survived. Patient 1 had no complication and was discharged 5 days after admission while patient 7 had complications including ARDS, pulmonary candidasis, infection associated phagocytic syndrome (IAHS), and pressure sore required prolonged ventilator support and was discharged after 44 days of admission.

4. Discussion

The mortality rate of DSS could be high from prolonged shock, massive bleeding, delayed diagnosis, and improper treatment which leads to uncorrected shock, metabolic acidosis, severe GI or other organs bleedings, and multi-organ failures [2]. In our study, most cases had prolonged shock and massive bleeding with low Hct level. The referral was quite delayed since 4 patients were referred to our PICU 1 day after leakage stage, whereas the other 4 were referred on day of leakage after fluid resuscitation but inadequate management of blood transfusion. Although some patients still had fever all were in leakage stage and were in prolonged shock represented by initial laboratory findings including high creatinine level (>1 mg%), and base excess >-10, indicating renal insufficiency and severe metabolic acidosis (Table 3). The mechanism of shock in DSS is not well understood. Generally, shock associated with DSS is caused by inadequate preload from vascular leakage into the third space [14] and massive bleeding [15]. All of our cases had massive pleural effusion either right (n = 3) or bilateral (n = 5) on admission indicating massive fluid leakage in the third space [16]. Hemoconcentration (rising of Hct >20% of baseline Hct) is one of the ominous sign of plasma leakage, however, there were only two patients with hemoconcentration. This is explained by active and massive bleeding in all patients except one and inadequate blood transfusion. The combination of fluid resuscitation and transfusion of blood components was crucial since hemoglobin is more important in transportation of oxygen to the tissue. Interestingly, initial CVP was high with median of 15 mmHg, even though the patients were in shock state and still required fluid and/or blood component resuscitation to maintain their vital signs. This may be explained by two reasons including elevated intrathoracic pressure due to positive ventilator support and massive pleural effusion, and elevated intra-abdominal pressure due to massive ascites especially when the catheter was in the inferior vena cava assessed from the femoral vein. Heart rate was elevated in all due to the compensation in response to shock. CT ratio by chest film was not increased in most patients, suggesting that there was no fluid overload causing cardiomegaly at the time of admission. The left ventricular end-diastolic volume index (LVEDVI) and %LVEDD were normal to low in most patients. These indicated that effective intravascular volume or preload was not adequate in most patients [17]. Wali et al. reported 17 adult patients with mean age of 29.76 years (range 14–58 years) including 8 of 17 with DSS and found that all had decreased LVEF and LVFS by echocardiography and radionucleotide ventriculography performed within 3 days of admission [5]. Kabra et al. reported decreased LVEF in 16.7% of children with DHF. [5] Khongphatthanayothin et al. reported significant lower LVEF during toxic stage

by echocardiography performed 4.6 ± 3.0 h after the diagnosis of DHF [7]. However, in that study, there was no patient in DSS grade 4. Khongphatthanayothin et al. reported decreased LVEF (<50%) in 9 of 25 children with DHF (only grade 1–3) [8]. Recently, Salgado et al. 11 patients of 102 dengue viral infections had mild to severe myocardial involvement including bradycardia, tachycardia, pericardial effusion, and diastolic function [18]. Unlike previous reports, LV systolic function represented by LVEF and LVFS in this study was normal in most patients. Only one patient had low LVEF and LVFS (LVEF 47% and LVFS 23%). This could be explained by two reasons, first, some patients had inotropic support from the beginning and at the time performing the echocardiography and, second, all patients had aggressive fluid resuscitation at the time of echocardiography to maintain their BP. As a general rule, systolic function assessed by EF and FS are preload dependent. The EF and FS may be compensated during aggressive fluid replacement. The CO and CI were still maintained during the shock state, however, the SVI was low in most cases (6 of 8 had SVI <40 mL/m^2/beat, table 4). The reason that CO and CI could be maintained was compensation by high HR. Interestingly, low SVRI was found in 6 of 8 cases. This finding suggested that in DSS, one of the mechanisms responsible for shock was vasodilatation causing low SVR like in septic shock. The low BP inspite of high CVP as shown in patient 7, may also suggest the role of the low SVR in explaining shock. We believed that vasopressor along with inotropes may have some roles in DSS and should be used along with appropriate fluid management in order to maintain blood pressure along with stroke volume and cardiac output. The pediatric index of mortality in our cases by PIM 2 was calculated from the information collected at the time a patient was admitted to our PICU. PIM2 described how ill the patient was at the time of admission to the intensive care. The first value of each variable was measured within an hour of arrival in our ICU. The median PIM 2 prediction of mortality was high, median 13.6 (3.8–57.5), in which 3 of 8 had PIM 2 >20%, four had PIM 2 >10% and <20%, and one had PIM 2 <10%. In the same direction, PRISM III which collected the worst of the 17 physiologic variables over the first 24 hr of admission [9] had a high score, 16.5 [10–19]. PRISM score >10 had a significant higher mortality rate in pediatric cancer patients admitted in PICU [19]. In this study, only one patient had PRISM score <10 and this patient survived, whereas seven patients had PRISM score >10 and only one patient survived. These two scoring systems confirmed that our cases had severe illness at the time

of the admission and during the first 24 hr. Among six patients who died, only one patient had unstable vital signs for her entire admission of 3 days. She had high PRISM score (score = 19) and PIM of 34.6%. The other four patients died from their complications including superimposed infection, ARDS, and severe brain edema after having survived the acute phase of DSS. Interestingly, one patient, operated 6 months back for VSD, developed severe pulmonary hypertension and hypertensive crisis with low cardiac output. The increased pulmonary blood flow from large VSD may affect pulmonary vascular resistance and cause some degree of pulmonary vascular change that may be aggravated by DSS.

Of interest, most patients had ARF, hepatic failure, encephalopathy, and severe brain edema. The reason for developing ARF was from prolonged shock. However, hepatic failure may be either from severe dengue hepatitis or from prolonged shock. Although fulminant hepatic failure is a rare manifestation of DHF, but hepatic failure has been associated with DHF particularly during epidemics in Indonesia and Thailand [7]. Moreover, fulminant hepatitis in DHF has a very high mortality [20]. Encephalopathy may be caused by dengue encephalopathy due to direct viral invasion of brain [20] or by hepatic encephalopathy due to acute hepatic failure. Nevertheless, both hepatic failure and encephalopathy had some roles to explain high mortality in this study.

5. Conclusions

Dengue shock syndrome had a high mortality rate especially when associated with prolonged shock, acute renal failure, hepatic failure, and hepatic encephalopathy. Decreased preload from bleeding and vascular leakage into the third space play the important role in shock. However, decreased stroke volume and low systemic vascular resistance may be additional causes of shock.

5.1. Limitations of the study

Although the sample size in this study is small, they were all DSS grade 4 cases with severe bleeding, prolonged shock, and multi-organ dysfunction. Echocardiography was performed only in the first hour after admission at PICU with variable status of intravascular volume, inotropic support, and volume resuscitation. Continuous hemodynamic monitoring such as ultrasonic cardiac output monitors or pulse-induced contour cardiac output

would enhance our understanding of the hemodynamic changes in dengue patients.

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