Original article

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Association of fluid overload with mortality in pediatric intensive care unit

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Abstract

***Objective*: To determine association of fluid overload with mortality in critically ill patients in Pediatric Intensive Care Unit.**

***Design*: This was a case-control study.**

***Settings*: Pediatric Intensive Care Unit of Sanglah Hospital Denpasar, Bali in January 2013 to December 2014.**

***Patients and participants*: Samples were patients who had completed treatment in Pediatric Intensive Care Unit of Sanglah Hospital Denpasar. Data was taken from medical records by simple random sampling technique both in the case and control groups. The cases were non-survivors and controls were survivors.**

***Intervention*: Observation made on fluid overload, defined as the fluid accumulation more than 10%.**

***Results*: Total of 120 children were examined in this study, which consisted of 60 samples for both case and control groups. The mean percentage of fluid accumulation was significantly higher in the case group (12.9±7.9%) compared to control (-1.4±8.2%), with mean difference 9.4% (95% CI:5.4-13.3; p<0.001). Fluid overload was associated with mortality (OR 11.5; 95% CI:3.7-35.6; p<0.001).**

***Conclusions*: Fluid overload is associated to and a risk factor for mortality in critically ill patients in pediatric intensive care unit. Fluid accumulation is higher in the non-survivors than survivors.**

Key words: Fluid overload, mortality, children.

Introduction

Fluid management is very important in the management of critically ill children. Fluid management is essential to maintain intravascular volume and organ perfusion. (1-4) One important consequence of fluid given in critically ill patients is fluid overload. (1,3,5-9) Recent studies indicate that fluid overload contribute to adverse outcomes in critically ill patients such as acute respiratory distress, acute lung injury, sepsis, acute pulmonary edema, acute kidney injury (AKI), encephalopathy, as well as post surgery treatment. (1-3,6,8)

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Study by Vaara in 283 adult patients admitted to the intensive care unit with renal replacement therapy showed 26.9% experienced fluid overload. (6) Study by Sutherland in 297 children admitted to the pediatric intensive care unit (PICU) and require renal replacement therapy showed 48.5% of samples had fluid accumulation >10%, (2) while there was very limited data or study of fluid overload in pediatric intensive care units in Indonesia.

Definition of fluid overload in critically ill patient is still defined in a wide variation, but generally implies an accumulation of fluid which resulting in pulmonary edema or peripheral edema. (1) Daily fluid balance refers to the difference of all fluid intake and output in one day, including insensible water losses (IWL). The cumulative fluid balance refers to fluid balance over a period of time. (1) The percentage of fluid accumulation was calculated from the cumulative fluid balance divided by weight when enter the intensive care unit. Some studies showed a cut off 10% were associated with increased of mortality. (1,6,8)

Some instruments or prognostic scoring systems designed to assess the possibility of mortality in critically ill children admitted to the pediatric intensive care unit. One of the instruments was the

pediatric logistic organ dysfunction (PELOD) score. The higher the PELOD score indicates the increased of mortality likelihood. (10) The occurrence of fluid overload in critically ill children with moderate or high PELOD scores would likely associated with increased of morbidity and mortality.

Methods

This was a case-control study. Target population in this study were critically ill children in pediatric intensive care unit, while accessible population were critically ill children in Pediatric Intensive Care Unit (PICU) of Sanglah Hospital, Denpasar, Bali.

Samples were patients who had completed treatment in Pediatric Intensive Care Unit of Sanglah Hospital, Denpasar, Bali during January 2013 to December 2014. Data was recorded from medical records using simple random sampling technique in both groups, case and control group to meet the required sample size. Sample frame obtained from mortality registers and admission registers in PICU of Sanglah Hospital. Determination of the minimum sample size based on unpaired case-control formula. (11-13) The minimum sample size for each case and control group was 59 patients. Inclusion criteria was patients who had completed treatment in PICU of Sanglah Hospital, Denpasar, Bali, hospitalized (in PICU) more than 48 hours, and PELOD score ≥10 at admission in PICU. Exclusion criteria was patients with incomplete medical records.

The independent variable in this study was fluid overload and the dependent variable was mortality. Fluid overload was defined as cumulative fluid accumulation more than 10%. Fluid accumulation percentage was calculated based on formula. (1,3,6,8)

Fluid accumulation (%) = (Fluid intake [L] - Fluid output [L]) / PICU admission weight [Kg] x 100%.

The calculation of PELOD score in each patient based on value of six major variable scores such as neurological, cardiovascular, renal, respiration, hematology, and liver function. Each variable had a score of 0, 1, 10 or 20. The maximum score for each variable was 20 and the maximum PELOD score was 71.

The study had been approved by The Ethics Committee of Medical School of Udayana University/Sanglah Hospital, Denpasar, Bali.

Data were entered into a computer program, then chi-square and bivariat test were used to determine the association and odds ratio between fluid overload and mortality. In addition, unpaired t test was used to determine the mean differences of fluid accumulation percentage and PELOD scores between the case and control group, and if the data were not normally distributed, the Mann Whitney test was used.

Results

A total of 120 samples were collected in this study, which consisted of 60 samples for the non-survival group (case) and 60 samples for the survival group (control). In this study, there was no significant differences in median PELOD scores between the case and control group (p=0.882). Meanwhile, there was significant differences in the mean fluid accumulation percentage between the case and control group, with mean difference 9.4% (95% CI:5.4-13.3; p<0.001). Characteristics of sample were shown in **Table 1**, and the analysis of PELOD score and cumulative fluid accumulation based on patient outcomes in **Table 2**. The distribution of the percentage of cumulative fluid accumulation based on patient outcomes was shown in **Figure 1**.

Based on chi-square test, fluid overload and mortality showed significant association (OR 11.5; 95% CI:3.7-35.6; p<0.001) as shown in **Table 3**.

Discussion

Some prognostic scoring systems were designed to assess the mortality likelihood in critically ill children. Study by Salim, et al (10) in PICU of Sanglah Hospital showed that pediatric logistic organ dysfunction (PELOD) daily scores could be used to predict mortality in critically ill children in PICU. In their study, moderate PELOD scores (10-19) and high PELOD scores (≥20) were associated with an increased risk of mortality with a RR of 2.3 (95% CI:1.09-5.02) and RR 3.3 (95% CI:1.01-10.6). (10) Our study showed no significant difference of PELOD scores between the case (median 12 [11-32]) and control groups (median of 12 [11-31]), p=0.882. This result indicated that at the time of admission in PICU, the risk for mortality was not different in both groups.

Based on chi-square test and OR calculations in this study, there was significant association between fluid overload and mortality (OR 11.5; 95% CI:3.7-35.6; p<0.001). This result indicated that mortality likelihood patients in PICU with fluid overload 11.5 times higher than patients without fluid overload. This study also found that the mean of cumulative fluid accumulation percentage was significantly higher in non-survivor group

(7.9±12.9%) compared with survivor group (-1.4±8.2%), mean difference 9.4% (95% CI:5.4-13.3; p<0.001). These results were consistent with several previous studies in both adults and children populations.

Multicenter prospective observational study in Finnish by Vaara, et al (6) in 283 adult patients in ICU with renal replacement therapy, found that fluid overload increased the risk of mortality with OR 2,6. Similar result was shown in a prospective multicenter observational study in San Diego, California by Bouchard, et al (8) in 618 adults with critical illness, which found higher percentage of fluid accumulation in non-survivor (7.1±9.1%) compared with survivor (4.9±8.4%) (p= 0.01). The study also found that fluid overload was associated with mortality in patients with AKI (OR 3.14; 95% CI:1.18-8.33).

Prospective cohort studies in Brazil by Silva, et al (14) in 479 post-surgical adult patients in ICU showed that fluid accumulation was higher in non-survivors than survivors (p<0.001). In addition, it also showed that fluid overload was a risk factor for mortality (OR 1.024) for every 100 ml of fluid accumulation (95% CI:1.007-1.0041; p=0.006). (14)

Single-center retrospective study in Texas by Arikan, et al (3) conducted in 80 pediatric patients (mean age 58.7±73 months) in the PICU showed that mean fluid accumulation percentage was higher in non-survivors (15.9±10.3%) than survivors (13.7±10%) group, even though this result was not statistically significant. Prospective multicenter observational study in the United State of America by Sutherland, et al (2) in 297 critically ill children in PICU and required continuous renal replacement therapy showed that fluid accumulation percentage was significantly higher in non-survivors than survivors group (23±23% vs 12.5±25.7%; p<0.001). It also showed that fluid overload was a risk factor for mortality (OR 8.5; 95% CI:2.8-25.7; p<0.001). (2)

Multicentre retrospective study in the United States of America by Abulebda, et al (15) in 317 pediatric patients with septic shock in PICU showed that cumulative fluid accumulation was significantly higher in non-survivors of 19.5% (10.5-40.1%) than survivors group of 6.5% (-1.3%-14.6%), p<0,001. Similar results were showed in a retrospective cohort study in Dallas by Bhaskar, et al (16) in 115 pediatric patients in PICU. This study showed on third day of treatment the mean cumulative fluid accumulation of 14.8±2.3% in non-survivors group and 6.4±0.7% in survivors group (p=0.002), and on the seventh day was 18.6±2.4% in non-survivors group and 7.5±0.6% in survivors group (p<0.001).

Our study result combining with previous studies showed the importance of fluid monitoring in critically ill patients in the intensive care unit. Monitoring fluid properly to avoid fluid overload should be one of the important focus to prevent morbidity and mortality on critically ill patients.

Limitations of our study: fluid accumulation was inaccessible prior to admission in pediatric intensive care unit, which can affect the cumulative fluid accumulation. Another limitation was the calculation of fluid accumulation obtained from report of intake and output records that could encountered an error on the counting process, although this had been minimized by doing a recount on any data collected. In addition, our study was retrospective, single centre study with all the limitations of retrospective study.

Conflict of interest

The authors affirm no conflict of interest on this study.

Table 1. Characteristics of sample

Variables	Non-survivors	Survivors
Male, n (%)	37 (61.7)	35 (58.3)
Median age, month (minimum-maximum)	8 (1-144)	11.5 (1-142)
Major problems/diagnosis, n (%)		
Neurology	22 (36.7)	19 (31.7)
Cardiology	5 (8.3)	8 (13.3)
Respirology	13 (21.7)	9 (15)
Gastro-hepatology	3 (5)	1 (1.7)
Tropical infections	8 (13.3)	9 (15)
Hematology-oncology	4 (6.7)	3 (5)
Nephrology	3 (5)	1 (1.7)
Nutrition	1 (1.7)	2 (3.3)
Endocrinology	0 (0)	1 (1.7)
Surgery	1 (1.7)	7 (11.7)

Table 2. Analysis of PELOD scores and cumulative fluid accumulation based on patient outcomes

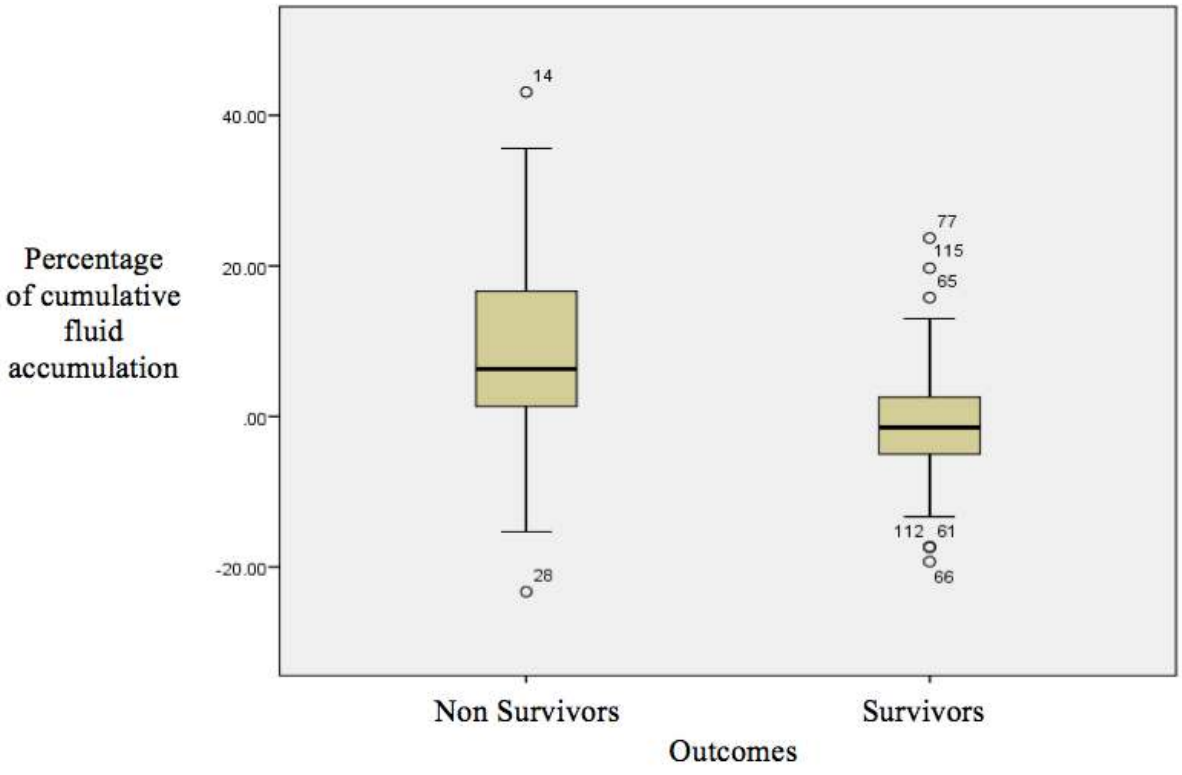
Variable	Non-survivors (cases)	Survivors (controls)	Mean differences (95% CI)	p value
Median PELOD score (minimum-maximum)	12 (11-32)	12 (11-31)	-	0.882*
Mean of cumulative fluid accumulation, %±SD	7.9±12.9	-1.4±8.2	9.4 (5.4-13.3)	<0.001**

Legend: *=using Mann Whitney test; **=using independent t-test.

Table 3. Bivariate analysis between fluid overload with mortality

Variable	Outcomes				p	OR	95% CI
	Non survivors	%	Survivors	%			
Fluid overload							
Yes	27	45	4	6.7	<0.001	11.5	3.7-35.6
No	33	55	56	93.3		ref	
Total	60	100	60	100			

Figure 1. The distribution of the percentage of cumulative fluid accumulation based on patient outcomes



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