Original Article

The alteration of renal function in sepsis and septic shock patients in pediatric intensive care unit

Feiby Julianto, Adrian Umboh, Suryadi Tatura

Abstract

Background Sepsis is a commonly seen emergency case in the pediatric intensive care unit.[1] Severe sepsis mortality rate in developed country andin developing country such as Indonesia are 9% and 50%-70%, respectively-. Furthermore, the mortality rate in septic shock is 80%.[2] Several researches documented increasing rate of acute kidney injury (AKI) incidence correlated with sepsis. Clinical intervention identification may decrease AKI and sepsis incidence.

Objective To identify the correlation between incidence of AKI in sepsis and in septic shock patients who was treated in pediatric intensive care unit (PICU)

Methods A cross sectional study was performed in 37 patients diagnosed as sepsis according ACCP/SCCM criteria for children aged 1 month to 13 years. The study was conducted in Pediatric Department, Prof. Dr. R.D. Kandou hospital from April 2009 to June 2009.

Results From 37 sepsis patients, 27 were boys and 10 were girls. In the sepsis group (n=27) 10 had AKI, and in the septic shock group (n=10) had AKI. Phi correlation coefficient applied to statistically analyzed sepsis in correlation with AKI (creatinin serum and GFR). Significant Phi correlation coefficient was (r) = 0,117; p > 0,05. (<)

Conclusions The study concludes that there is no correlation of renal function impairment with sepsis and septic shock. [Paediatr Indones. 2011;51:89-93].

Keywords: sepsis, septic shock, acute kidney injury

Sepsis is an emergency situation commonly seen in the pediatric intensive care units. Delayed diagnosis and treatment may deteriorate the condition toward severe sepsis, septic shock, and multiple organ failure.[1] Severe sepsis mortality in developed country has decreased to 9%. However in developing country such as Indonesia, sepsis mortality rate is still high, 50% to 70%, and if it persists to septic shock and multiple organ failure, the mortality rate raises to 80%.[2]

Acute kidney injury (AKI) is clinical syndrome which suddenly occurs caused by alteration of renal function as a consequence of unable to resist the balanced of water and electrolytes. This condition can result to nitrogen retention (ureum and creatinine) and non nitrogen product that normally excreted by kidney. It occurs in 2-3% children who admitted to hospital.[1,2] Generally, diagnosis is made while creatinine (Cr) or blood urea nitrogen (BUN) increases.[2] Glomerulus filtration rate (GFR) is a useful index to evaluate renal function. Decreasing of GFR is a sign of significant abnormality renal

From the Department of Child Health, Medical School, Sam Ratulangi University, Manado, Indonesia.

Reprint requests to: Feiby Julianto, MD, Department of Child Health, Medical School, Sam Ratulangi University, Prof. R.D. Kandou General Hospital, Jl. Raya Tanawangko, Manado 95263. Indonesia. Tel. 62-431-821652. Fax. 62-431-859091.

function. Creatinine serum concentration is an excessive examination used to evaluate renal function.[3]

AKI happens about 19% of sepsis patients, 23% of severe sepsis and 51% of septic shock. Combination of sepsis and AKI is a serious problem in United States, because sepsis associated with increased of AKI incidence.[6] Unfortunately, information of AKI in sepsis patients is still a few.[5] In a study, was done by Bagshaw and colleague, Hoste and colleagues, Neveu and colleagues, Van Biesen and colleagues, found that sepsis patient associated with AKI.[6,8-10] The purpose of this study was to evaluate impairment of renal function through examination of creatinine serum and GFR that was experienced by sepsis and septic shock patient in Intensive Care Unit (ICU).

Methods

This study was done by using analytic and descriptive observational study methods with cross sectional manner. Location of this study was Pediatric Intensive Care Unit of Prof. Dr. R.D. Kandou Hospital Manado from April to Juni 2009.

All pediatric patient with sepsis were clarified by ACPP and SCCM criteria. The sample were obtained based on inclusion criteria, as follows: 1) children aged 1 month-13 years, 2) parents or caretakers agreed to participate and filled the informed consent. The exclusion criteria were malnutrition, and severe dehydration. There were 27 children in sepsis, and 10 in septic shock. This study used 37 $\alpha = 0,05$, $\beta = 0,10$.

Sample was obtained in consecutive methods. In this study there were two variables (independent variable and dependent variable). Independent variables wer sepsis and septic shock. Dependent variables were creatinine serum and GFR. Data was taken by doing anamnesis, physical examination and laboratory examination. Anamnesis and physical examination were obtained by researcher on office hour. After office hour, the patients were examined by general physician on duty and reexamined by researches. Laboratory examination was done by hematologist. Anamnesis data included name, gender, age, address, parents/ caretaker identity, sign of

sepsis and septic shock. Physical examination ,when the patient arrived in hospital, consisted of body temperature (measured per rectal for 3 minutes), vital sign and shock sign (by blood pressure, pulse, respiration rates). Continued with collecting blood vein sample in EDTA for routine blood examination to sum number of stem cell. Creatinine serum examination and GFR were done twice while patient admitted to hospital and on 24 hours treatment

Sepsis is an evidence clinic of infection includes tachycardia (based on age), tachypnea (based on age), rectal body temperature ($> 38\ ^0$C or $< 36\ ^0$C), leukocyte $> 12.000/\mu$L or $< 4.000/\mu$L or stem cell $> 10\%$.[11]

Shock septic is sepsis syndrome with systemic hypotension. In other words, sepsis syndrome along with decreasing of organ perfusion signed by one of these criteria, as follows: 1)mentally disturb (irritable, lethargy, semi coma, coma), 2)oliguria (urine production < 1 ml/kg of body weight /hours), 3)hypoxemia PaO$_2$ < 75 mmHg, 4)capillary volume > 2 second, or 5)decreasing of peripheral sirculation.[11]

The impairment of renal function means suddenly decrease of renal function signed by decreased of GFR along with increased of creatinine blood above the normal value.[12]

Creatinine serum level, that excreted through renal tubule and filtrated by glomerulus, may indicate the impairment of renal function.[13]

GFR is the best way to predict renal function, counted by Schwartz's formula usinglevel of creatinine serum.[14]

In exclusion criteria, there were condition of malnutrition and severe dehydration. Malnutrition is a situation of severe malnutrition in child that caused by lower protein and energy concentration in daily food continuously. Based on CDC, malnutrition can be detected by comparing weight and height of the body < 70.[15] Meanwhile, severe dehydration can be detected based on 2 or more signs and symptom of severe dehydration. The anamnesis includes frequency of diarrhea more than 10 times in a day, frequent vomiting, thirstiness or couldn't take a drink, anuria for 6 hours and on physical examination the patient is in nervous or unconscious, tearless , dryness and concave of the eyes, dryness of the mouth and tongue, depth and fast to breath, decreasing of turgor, concave on fontanel and losing of the weight body more than 10%.[16]

Results

During the study period, we obtained 42 children, five sample were excluded from the study because of uncompleted data, therefore, the number of sample participated in this study was 37 children.

These 37 children consisted of 27 boys and 10 girls. There were 27 children in sepsis, and 10 in septic shock. The average age in study sample is 2.99 years old and standard deviation 3,94 years old in septic shock group.

From 37 study subjects there were five children with malnutrition in sepsis group and two children with malnutrition from septic shock group. Found that 2 child over nutrition in sepsis group and one child over nutrition in septic shock group.

Discussion

In this study, there were 37 children consisted of 27 boys and 10 girls. Distribution age in 37 children were

Table 1. Creatinine serum level when admitted to hospital

Creatinin	Sepsis		Total
	Sepsis	Septic Shock	
Normal	16	3	19
Increased	11	7	18
Total	27	10	37

Phi Coeficient correlation (r) = 0,260; p > 0,05

Table. 2. Creatinine serum level during treatment in hospital

Creatinin	Sepsis		Total
	Sepsis	Septic Shock	
Normally	15	5	20
Increased	12	5	17
Total	27	10	37

Phi Coeficient Correlation (r) = 0,050; p > 0,05

Table. 3. Level of GFR when admitted to hospital

LFG	Sepsis		Total
	Sepsis	Septic Shock	
Decreased	16	7	23
Normally	10	2	10
Increased	1	1	4
Total	27	10	37

Rho spearmen coeficient correlation (r) = -0,070; p>0,05

Table. 4. Level of GFR during treatment in hospital

LFG	Sepsis		Total
	Sepsis	Septic Shock	
Decreased	17	6	23
Normally	7	3	10
Increased	3	1	4
Total	27	10	37

Rho spearman coeficient correlation (r) = 0,020; p > 0,05
From the tables, it is shown that there is no correlation between level of creatinin, GFR and sepsis, septic shock patients.

between 2-3 years old. When admitted to hospital, there were 11 from 27 sepsis patients and seven from 10 septic shock patients who had increased in level of creatinine. On 24 hours treatment, there were 12 from 27 sepsis patient and five from 10 septic shock patient who had increased in level of creatinin serum, It is statistically low because of Phi coefficient Correlation (r) was 0,260; p > 0.05 when admitted to hospital and in 24 hours treatment, Phi Coefficient correlation (r) was 0.050; p > 0.05, it means that not all of patients with sepsis and septic shock will fall into kidney injury.

In this study, one of the factors that influenced of creatinine level was nutrition status (seven children with malnutrition). Based on literature said that creatinine associated to muscle mass.[4] In one study that observed creatinine level, found that 77 boys with malnutrition and 77 boys with good nutrition without any evidence of renal failure, had an average of creatinine serum in children with malnutrition was 0.42 (0.38-0.45). While creatinine serum in children with good nutrition was 0.51 (0.45-0.55). (p value < 0.01).[19]

In recent management of sepsis from ward to ICU stated that immediate diagnosis and treatment (in six hours) are important part to decrease the complication of renal in sepsis patient.[20] In sepsis, there are hypoxia process, hypercapnia and acidosis that can effect to organs, It also depends on how long and how severe the hypoxia process. Hypoxia makes hypoperfusion of blood to kidney and so can influence the renal function and change biochemical process. Decreased of GFR is a consequences to hemodynamic disturb (vascular), glomerular, and tubulus. These three factors have influenced each others.

In this study, there were 16 of 27 sepsis patients and seven of 10 septic shock patients who had decreased in level of GFR . Meanwhile, on 24 hour-treatment, there were 17 of 27 sepsis patients and six of 10 septic shock patients, who had decreased in level of GFR. Therefore, there was no correlation between GFR with sepsis and septic shock. From statistical test we can obtain Rho Spearman Coefficient correlation (r) = 0.020; p > 0.05 on 24 hours treatment. This means not all of the children, experience sepsis or septic shock, will fall into renal failure.

After reassessment of creatinine level after 24 hour- treatment only one patient had increased in level of creatinin. This means that renal failure is not simply experienced in stress situation like sepsis. This matter can be explained that there are many factors need to be involved to make renal failure like hypoxia with long duration and consequences of hypoxia to tissue (hipercapnia or acidosis), renal auto regulation factors as well as renal vasoactive factors (vasodilator and vasoconstrictor of renal).[5,21-23.]

In study by Hoste and colleague[8], stated that among 185 sepsis patients admitted to ICU, there were 16.2% experienced acute kidney injury on 24 hour-treatment. Factors associated to acute kidney injury were decreasing of blood pressure, metabolic acidosis, delayed liquid therapy, vasoactive drugs.

Study by Bagshaw and colleague[7], stated that among 1753 child patients > 12 years of age admitted to ICU, there were 833 patients (47,5%) with sepsis as contributing factor to acute kidney injury.. Contributing factors included post operation, hypovolemia, drugs intoxication, and cardiogenic shock. Identification patient in early stadium or initial of acute kidney injury and identification of risk factors associated to acute kidney injury can prevent to deterioration of kidney function.[17] If kidney vasoconstriction is severe and long-lasting, it will effect on and global hypoperfusion that can result in acute tubular necrosis. However this theory can not be applied in sepsis associated to kidney disease.[22] According to Venkatraman, primary strategic to prevent acute kidney injury in sepsis patient, by non pharmacologic (adequate hydration, maintain of mean arterial pressure, minimal contact to nephrotoxin) and pharmacologic are to increased blood flow or decreased oxygen used in kidney.[24]

In this study, after evaluated for 24 hours, restoration occured in kidney function, signed by decreasing of creatinine serum level in two septic shock patient and increasing of GFR. This result is caused by quick identification of sepsis patient, immediate treatment and fluid resuscitation/ hydration adequately in the beginning of sepsis/shock.

There is an evidence that in initial phase of kidney injury, caused by sepsis, dominant pathogenic factors are elevation of water and natrium reabsorbtion in tubulus.[22] Initial vasoconstriction phase of acute kidney diseases can be reversible, therefore optimal time is an important part in intervention. In conclusion, there is no correlation of renal function impairment with sepsis and septic shock.

References

1. Enrione MA, Powell KR. Sepsis, septic shock, and systemic inflammatory. In : Kliegman RM, Nelson EB, Jenson HB, Stanton BF, Editors. Nelson Textbook of Pediatrics. 18th Eds. Philadelphia : Elsevier Saunders, 2007;1094-9.

2. Setiadi TE. Penatalaksanaan syok septik pada anak. Banjarmasin: Bagian Ilmu Kesehatan Anak RSUD Ulin; 2005.

3. Hellerstein S, Berembom M, Erwin P, Wilson N, DiMaggio S. Creatinin for evaluation of glomerular filtration rate in children. Clin Pediatr. 2006;45:525-30.

4. The New York Times. Creatinine-serum [homepage on the internet]. Last update 2 December 2008; Review date 7 August 2009. Available from : http://health.nytimes.com/health/guides/test/creatinine-serum/overview.html

5. Schrier RW, Wang W. Acute renal failure and sepsis. N Engl J Med. 2004;351:159-68.

6. Bagshaw SM, Uchino S, Bellomo R. Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. Clin J Am Soc. Nephrol 2007;2:431-9.

7. Boffa JJ, Arendshorst WJ. Maintenance of renal vascular reactivity contributes to acute renal failure during endotoxemic shock. J Am Soc Nephrol. 2005;16:117-24.

8. Hoste EAJ, Lameire NH, Vanholder RC, Benoit DD, Decruyenaere JMA, Colardyn FA. Acute renal failure in patients with sepsis in a surgical ICU: predictive factors, incidence, comorbidity, and outcome. J Am Soc Nephrol. 2003; 14: 1022-1030.

9. Neveu H, Kleinknecht D, Brivet F, Loirat P, Landais P. Prognostic factor in acute renal failure due to sepsis: results of a prospective multicentre study. Nephrol Dial Transplant. 1996; 11: 293-9.

10. Van Biesen, Vanholden R, Lameire N. Defining acute renal failure : Rifle and beyond. Clin J Am Soc Nephrol. 2006;1: 1314-9.

11. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Kraus WA, *et al*. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest. 1992;101:1644-55.

12. Alatas H. Gagal ginjal akut. In : Alatas H, Tambunan T, Trihono PP, Pardede SO, editors. Buku ajar nefrologi anak. 2nd Ed. Jakarta: Balai Penerbit FKUI, 2002;p.490-506.

13. Heymsfield SB, Arteaga C, Mc Manus C, Smith J, Moffitt S. Measurement of muscle mass in humans : validity of the 24-hour urinary creatinine method. Am J Clin Nutr. 1983;37:478-94.

14. Alatas H. Pemeriksaan laboratorium pada penyakit ginjal. In : Alatas H, Tambunan T, Trihono PP, Pardede SO editors. Buku ajar nefrologi anak. Jakarta:. FKUI, 2002;51-72.

15. Hall JG, Allanson JE, Gripp KW, Slovotinek AM. Height and length. Hall JG, Allanson JE, Gripp KW, Slovotinek AM, editors. Handbook of physical measurements. 2nd ed. New York: Oxford University Press, 2007;15-29.

16. Divisi Gastroenterologi Lab/SMF Ilmu Kesehatan Anak FK Unair. Sindroma diare. In: Sudarmo SM, Soeparto P, Djupri LS, Rauh IGMRG, editors. Sindroma diare patofisiologi, diagnosis, penatalaksanaan. Surabaya: Divisi Gastroenterologi Lab/SMF Ilmu Kesehatan Anak FK Unair, 2004;41-1.

17. Ghani AA, Al Helal B, Hussain N. Acute renal failure in pediatric patients : etiology and predictors of outcome. Saudi J Kidney Dis Transplant. 2009;20(1):69-76.

18. Van Lente F, Suit P. Assessment of renal function by serum creatinine and creatinine clearance : glomerular filtration rate estimated by four procedures. Clin Chem. 1989;35 (12):2326-30.

19. Pankaj H, Arvind B, Punnett M, Ramakrishnan L. Effect of malnutrition on serum creatinine and cystatin c levels. Pediatr nephrol. 2007;22(10):1757-61.

20. Watson RS, Carcillo JA, Linde-Zwirble. The epidemiology of severe sepsis in children in the United States. Am J Respir Crit Care Med. 2003;167:695-701

21. Schor N. Acute renal failure and the sepsis syndrome. Kidney Int. 2002; 61: 764-76.

22. Shah SM. Kidney in sepsis-Part I. Inf Dis J Pakistan. 2008;17(4):123-6.

23. Oppert M, Engel C, Brunkhorst FM. Acute renal failure in patients with severe sepsis and septic shock – a significant independent risk factor for mortality : results from the German prevalence study. Nephrol Dial Transplant. 2008;23:904 - 9.

24. Venkataraman R, Kellum JA. Prevention of Acute renal failure. Chest. 2007;131 300-8.

25. Suharto. The recent management of sepsis from ward to ICU. Proceeding Book Perhimpunan Peneliti Penyakit Tropik dan Infeksi (PETRI). Surakarta: PETRI, 2007 ; 96-105.