RESEARCH ARTICLE

Urine D-dimer Level in Severe Preeclampsia-complicated Acute Kidney Injury: A Cross-sectional Study

Putri Mirani[1], Noroyono Wibowo[2]

Abstract

Introduction: Preeclampsia has become the most common glomerular-based kidney disease affecting up to 8% of normal pregnancies.[1–3] Thus, a worsening condition of preeclampsia will be related to an increasing risk of renal disease, particularly acute kidney injury (AKI).[1,2] Acute kidney injury has become the common renal disease complication due to severe preeclampsia with the incidence up to 5%.[4] This complication is mainly caused by thrombotic microangiopathy involving renal arteries, which can be observed with an increasing urine D-dimer level. This study aims to determine the urine D-dimer level in severe preeclampsia-complicated AKI.

Materials and methods: A cross-sectional study was conducted in Obstetric Emergency Unit and Obstetric Ward Unit, Cipto Mangunkusumo General Hospital, from January to April, 2013. Subjects were divided into two groups: severe preeclampsia-complicated AKI and normotensive pregnancy. The main outcome of this study was that urine D-dimer level was based on the cutoff point from receiver operating characteristic (ROC). The secondary outcomes were its sensitivity and specificity. Statistical analysis was performed using Mann–Whitney and Spearman correlation tests. Data were analyzed using SPSS 20.0.

Results: There were 65 subjects collected during the study and divided into two groups: 35 patients with severe preeclampsia-complicated AKI and 30 patients with normotensive pregnancy. There was a significant increase in the urine D-dimer level in patients with severe preeclampsia-complicated AKI compared with patients with normotensive pregnancy (2503 ng/mL vs 236.2 ng/mL; $p = 0.001$). Based on the ROC, the cutoff point for the urine D-dimer level was >818 ng/dL with area under the ROC curve was 0.819 (81.9%), sensitivity 80%, and specificity 73%.

Conclusion: The urine D-dimer level significantly increased in severe preeclampsia-complicated AKI with a cutoff point of >818 ng/dL, sensitivity 80%, and specificity 73%.

Keywords: Acute kidney injury, Severe preeclampsia, Urine D-dimer.

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Introduction

Hypertensive complication during pregnancy remains a major problem increasing maternal–neonatal mortality and morbidity, particularly manifest as preeclampsia.[1,2,5,6] It has become the most common glomerular-based kidney disease affecting up to 8% of normal pregnancies.[1–3] Thus, a worsening condition of preeclampsia is related to an increasing risk of renal disease, particularly acute kidney injury (AKI).[1,2]

Acute kidney injury has become the common renal disease complication due to severe preeclampsia with the incidence up to 5%.[4] This complication is mainly caused by thrombotic microangiopathy involving renal arteries.[1,3,6] It began as an imbalance process of the coagulation system between prostacyclin and thromboxane, thus resulting in the circulation of thrombin in the blood vessels.[7,8] As the coagulation process continues, the circulating thrombin disintegrated and released fibrin degradation products, including D-dimer, thereby increasing the D-dimer level.[6–8]

Severity of thrombotic microangiopathy involving renal arteries due to worsening preeclampsia can be observed clinically as AKI and biochemically as increasing urine D-dimer level. This study aims to determine the urine D-dimer level in severe preeclampsia complicated with AKI.

Materials and Methods

This was a cross-sectional study conducted in Obstetric Emergency Unit and Obstetric Ward Unit, Cipto Mangunkusumo General Hospital, from January to April 2013. Subjects were divided into two groups: severe preeclampsia-complicated AKI and normotensive pregnancy. Inclusion criteria for the severe preeclampsia group were singleton live intrauterine pregnancy, gestational age >20 weeks, diagnosed as severe preeclampsia/eclampsia with/without HELLP syndrome-complicated AKI, and normal body temperature. Inclusion criteria for the control group were singleton live intrauterine pregnancy, gestational age >20 weeks, normotensive, and normal body temperature. Exclusion criteria for both groups were having history of liver disease, having history of hematology and coagulation disorder, having history of renal disease previously, was using anticoagulant and thrombolytic agents for treatment, diagnosed as disseminated intravascular coagulation, unwilling to participate in study, and sample damage. This is a pilot study, therefore used a minimal sample size of 30 subjects for each group.

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Table 1: Subject characteristic in urine D-dimer level in severe preeclampsia-complicated AKI study

Subject characteristics	*Severe preeclampsia-complicated AKI (n = 35)*	*Normotensive pregnancy (n = 30)*
Age (years)	30 ± 5	28 ± 5
Gestational age (weeks)	32 (23–40)	36 (23–41)
Primiparity (%)	13 (37.1)	14 (50)
Systolic blood pressure (mm Hg)	170 (160–240)	120 (100–130)
Diastolic blood pressure (mm Hg)	103 (100–140)	75 (60–90)
Temperature (°C)	36.6 (36–37)	36.6 (36.4–36.8)
Diuresis (mL/kg body weight/hour)	0.3 ± 0.08	1.54 ± 0.30
Urine creatinine (mg/dL)	73.7 (10.4–203.4)	51.5 (37–51.6)
Plasma creatinine (mg/dL)	1.7 ± 1.8	0.7 (0.5–0.8)
Leukocyte (/mm^3)	18,717 ± 8555.2	9,050 (6,660–14,600)
Plasma D-dimer (ng/mL)	2,472 ± 1,385	2,525 ± 1,607
Urine D-dimer (ng/mL)	2,503 (106–4,290)	788 ± 1,179

Table 2: Mode of delivery and neonatal outcome between two groups

Neonatal outcome	*Severe preeclampsia-complicated AKI (n = 35)*	*Normotensive pregnancy (n = 30)*	*p*
Mode of delivery			
Spontaneous [*n* (%)]	16 (30.1)	14 (46.6)	>0.05*
Cesarean section [*n* (%)]	19 (54.9)	16 (53.3)	
Birth weight (g) [median (min–max)]	1,970 (600–3,265)	2,665 (600–4,000)	0.03†
Apgar score minute 1 [median (min–max)]	7 (1–9)	9 (1–9)	0.03†

*Chi-square test
†Mann–Whitney test

The main outcome of this study was that urine D-dimer level was based on the cutoff point from receiver operating characteristic (ROC). The secondary outcomes were sensitivity and specificity. Statistical analysis was performed using Mann–Whitney and Spearman correlation tests. Data were analyzed using SPSS 20.0. This study had been approved by the Ethical Committee Faculty of Medicine University of Indonesia/RSCM with ethical approval no. 746/H2.F1/ETIK/2012.

Results

There were 65 subjects collected during study and divided into two groups: 35 patients with severe preeclampsia-complicated AKI and 30 patients with normotensive pregnancy. All subject characteristics are shown in Table 1.

Table 2 shows the mode of delivery and neonatal outcome between two group studies. There was no significant difference in the mode of delivery, but there was a significant difference in the neonatal outcome. Neonatal delivered from severe preeclampsia-complicated AKI group were smaller in weight (median 1970 g) and were having mild asphyxia (media Apgar score 7).

There was a significant increase in the urine D-dimer level in patients with severe preeclampsia-complicated AKI compared with patients with normotensive pregnancy (2503 ng/mL vs 236.2 ng/mL; $p = 0.001$). Based on the ROC, the cutoff point for the urine D-dimer level was >818 ng/dL with area under the ROC curve (AUC) was 0.819 (81.9%), sensitivity 80%, and specificity 73%. receiver operating characteristic with the cutoff point from AUC is shown in Figure 1.

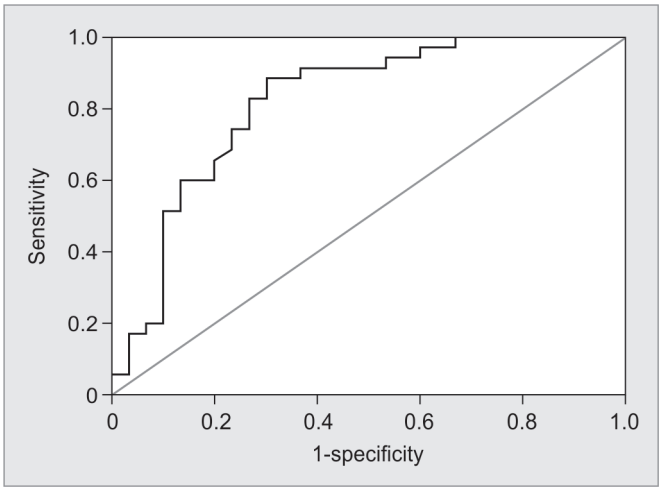

Fig. 1: Receiver operating characteristic of the urine D-dimer level in severe preeclampsia-complicated acute kidney injury (AKI)

Discussion

Preeclampsia has become the most common hypertensive complication during pregnancy risking not only cardiovascular system but also renal function.[2,5,6] Thus, the worsening condition of preeclampsia should be detected accurately and managed carefully. Based on the subject characteristic, subjects in the severe preeclampsia-complicated AKI group were significantly different from normotensive groups, especially in blood pressure, diuresis,

urine, and plasma creatinine level. Blood pressure and creatinine level (both urine and plasma) were significantly higher, whereas diuresis in severe preeclampsia-complicated AKI was significantly lower. Hypertensive characteristic in this study corresponds to American College of Obstetricians and Gynecologists (ACOG) criteria for severe preeclampsia, while diuresis and creatinine level correspond to risk, injury, failure, loss of kidney function, and end-stage kidney disease (RIFLE) and acute kidney injury network (AKIN) criteria for AKI.[6,9–12]

In this study, the urine D-dimer level was significantly higher in severe preeclampsia-complicated AKI compare with normotensive group (2503 ng/mL vs 236.2 ng/mL; $p = 0.001$). This condition was related to fibrin accumulation in glomerular endothelial cells causing vascular permeability disruption, thus increasing D-dimer excretion through urinary process. Therefore, increased urine D-dimer level can be used as diagnostic tools for diagnosis of severity of worsening preeclampsia, particularly severe preeclampsia-complicated AKI.[9,13] Other condition related to severity of preeclampsia was clinical symptoms of oliguria found in the severe preeclampsia-complicated AKI group. This was showing severe glomerular endothelial disruption leading to AKI.[2,3,6]

Based on the ROC, the cutoff point from AUC for urine D-dimer level was 0.819 (81.9%), with sensitivity 80% and specificity 73%. This value can be used as noninvasive diagnostic tools (AUC > 80%) and can predict the worsening condition in severe preeclampsia-complicated AKI.

This study was a prior study. There were some limitations regarding sample size being used in this study. Thus, we recalculated the power of study to minimal mean level of urine D-dimer difference and standard deviation, which resulted in β-value 1.3 that corresponds to power of 90–95%. It was shown that sample size being used in this study was qualified enough to compare urine D-dimer level between two groups. Further study should be conducted to generalize the cutoff point in large population, so that it can be compared with renal biopsy as a gold standard for diagnosing thrombotic microangiopathy due to preeclampsia and to identify other factors causing AKI besides endothelial disruption due to fibrin accumulation on glomerular endothelial cells.

Conclusion

The urine D-dimer level significantly increased in severe preeclampsia-complicated AKI, with the cutoff point of >818 ng/dL, sensitivity 80%, and specificity 73%.

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