

## Clinical and Laboratory Profiles Relationships of Preeclampsia-eclampsia Patients with Maternal Mortality in Dr. Soetomo Hospital, Surabaya

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### ABSTRAK

*Preeklamsia-eklamsia adalah salah satu komplikasi yang paling umum dari kehamilan dan salah satu penyebab tertinggi kematian ibu di negara-negara berkembang. Ini menjadi penyebab utama kematian ibu yang sulit untuk mencegah, kecuali kondisi klinis ibu dengan profil laboratorium dapat diidentifikasi dengan cepat dan dipahami dengan baik. Tujuan dari penelitian ini adalah untuk mempelajari hubungan antara profil klinis dan laboratorium preeklamsia-eklamsia pasien dengan kejadian kematian ibu. Penelitian ini merupakan studi retrospektif observasional analitik pada pasien dengan preeklamsia-eklamsia yang dirawat di rumah sakit Dr. Soetomo antara periode Januari 2009 sampai Desember 2011. Data diambil dari catatan medis RS Dr. Soetomo Surabaya. Variabel yang akan dinilai adalah kondisi klinis (edema paru, edema serebral, perdarahan intraserebral, sindrom HELLP, DIC, gagal ginjal dan pelepasan retina) dan laboratorium (hemoglobin, leukosit, hematokrit, trombosit, GDA, SGOT, SGPT, BUN, SK, Na, K, albumin, LDH), dan hasil (hidup atau mati). Data diolah dengan menggunakan software SPSS. Pada masing-masing variabel dilakukan uji regresi logistik. Hasil: Selama periode 3 tahun ditemukan 247 kasus preeklamsia-eklamsia dengan angka kematian ibu 10,5%. ALT > 40 U / L ( $p = 0,001$ ) dan jumlah trombosit < 150.000 / uL ( $p = 0,0001$ ) memiliki hubungan yang signifikan dengan kejadian kematian ibu pada sindrom HELLP. Kreatinin serum > 1,2 mg / dL ( $p = 0,0001$ ) memiliki hubungan yang signifikan dengan kejadian kematian ibu pada ARF. Edema paru memiliki hubungan yang signifikan dengan kejadian kematian ibu ( $p = 0,0001$ ). Jumlah trombosit < 150000 / uL memiliki hubungan yang signifikan dengan kejadian kematian ibu akibat edema otak ( $p = 0,0001$ ). Sebagai kesimpulan, gambaran klinis pasien preeklamsia-eklamsia yang meninggal di rumah sakit Dr. Soetomo Surabaya berkaitan dengan gambaran laboratoris mereka (MOG 2012;20:35-39)*

**Kata kunci:** preeklamsia, eklamsia, profil laboratoris, kematian ibu

### ABSTRACT

*Preeclampsia-eclampsia is one of the most common complications of pregnancy and one of the highest causes of maternal mortality in developing countries. It becomes a major cause of maternal deaths that are difficult to prevent, unless the clinical condition of the mother with laboratory profiles can be identified quickly and well understood. The objective of this research was to study the relationship between clinical and laboratory profiles of preeclampsia – eclampsia patients with incidence of maternal mortality. This study was a retrospective observational analytic studies in patients with preeclampsia-eclampsia were treated in Dr. Soetomo hospital between January 2009 and December 2011. Data were retrieved from Dr. Soetomo Hospital Surabaya medical records. The assessed variables were clinical conditions (pulmonary edema, cerebral edema, intracerebral hemorrhage, HELLP syndrome, DIC, renal failure and retinal detachment) and laboratory (hemoglobin, leukocytes, hematocrit, platelets, GDA, SGOT, SGPT, BUN, SK, Na, K, albumin, LDH) and the outcomes (alive or dead). Data were processed using SPSS software. On each of the variables logistic regression test was performed. It was found that during the 3-year period there were 247 cases of preeclampsia-eclampsia with maternal mortality rate 10.5%. ALT > 40 U/L ( $p = 0.001$ ) and Platelets count <150.000 / $\mu$ L ( $p = 0.0001$ ) had a significant relationship with the incidence of maternal mortality in HELLP syndrome. Creatinine serum > 1.2 mg/dL ( $p = 0.0001$ ) had a significant relationship with the incidence of maternal mortality in ARF. Pulmonary edema had a significant relationship with the incidence of maternal mortality ( $p = 0.0001$ ). Platelets count <150000 / $\mu$ L had a significant relationship with the incidence of maternal death in cerebral edema ( $p = 0.0001$ ). In conclusion, clinical profiles in preeclampsia-eclampsia patients who died in Dr. Soetomo Hospital, Surabaya, has correlation with their laboratory profiles. (MOG 2012;20:35-39)*

**Keywords :** preeclampsia, eclampsia, laboratory results, maternal mortality

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### INTRODUCTION

Preeclampsia is a pregnancy-specific syndrome in the form of reduced organ perfusion due to vasospasm and

endothelial activation, generally occurs in pregnancy over 20 weeks. Proteinuria is an important sign of preeclampsia, and if there is no proteinuria, the diagnosis is questionable.<sup>2</sup>

Preeclampsia-eclampsia is one of the most common complications of pregnancy and one of the highest causes of maternal mortality (15-20%) in developing countries. The most frequent cause of maternal death in the case of pre-eclampsia is HELLP syndrome (hemolysis, elevated liver enzymes and low platelets count) and pulmonary edema.<sup>1</sup> In general, the lower of the platelet count, the greater the maternal or infant mortality rate.<sup>2</sup> Sibai et al, get 49% of patients with pulmonary edema had significant renal impairment and 54% had hypoalbuminemia.<sup>6</sup> Contributions preeclampsia-eclampsia on maternal mortality in Indonesia by an average of 12%. While maternal mortality due to preeclampsia-eclampsia in East Java reported 117 (28.2%) of 414 maternal deaths in 2007.<sup>3</sup> In Dr. Soetomo Hospital disease is the highest cause of maternal death in the amount of 38.54%.

In Preeclampsia process begins with an abnormal trophoblast invasion of the spiral arteries, causing the arteries to vasospasm. It also found the tunica media hyperplasia and thrombosis, so the diameter of the spiral arteries 40% smaller than normal pregnancy causing blockage can be partial or total. If it lasts longer then it would result in reduced uteroplacental circulation ischemia can develop into the placenta. Hypotheses are important in the pathogenesis of preeclampsia is the presence of compounds produced uteroplacental tissues into maternal circulation and cause endothelial damage. Changes in endothelial function is considered as the main cause of preeclampsia.<sup>6</sup>

The existence of vasospasm, ischemia and endothelial dysfunction resulted in changes in various organs in the body. Changes that occur in the liver in the form of periportal necrosis, mikrotrombi and fibrin deposits were many sinusoid. Obstruction of the circulatory system resulting in swelling of the liver so that the capsule is stretched Glissoni participate. It causes a pain in the stomach. In laboratory tests found the hemolysis, elevated liver enzymes and low platelets count, which was then called HELLP syndrome.<sup>10</sup> Changes that occur in the brain is the cerebral hiperperfusion. The possibility of the loss of autoregulation of cerebral blood flow that manifests as a decrease in vascular resistance. This would lead to interference with the brain's blood vessels form ischemia, thrombosis, minimal bleeding that occurs at the same time, the result would be hyperemia and edema.<sup>7</sup> Clinical manifestations encountered form of cerebral edema and intracerebral hemorrhage. In laboratory tests found the thrombocytopenia and coagulation system disorders.<sup>4</sup>

In pulmonary disorders such as pulmonary edema occurs, which is a condition in which an increasing number of interstitial lung fluid and lung alveoli are

beyond the ability of the lymphatic system drainage. This occurs due to increased capillary permeability due to damage to the pulmonary vascular endothelium, which are due to the preeclampsia. Onset of pulmonary edema interfere with the oxygenation in the lungs causing severe hypoxemia characterized by falling PO<sub>2</sub>, causing severe hypoxia.<sup>11</sup> In laboratory tests found an increase in creatinine serum and hypoalbuminemia.<sup>6</sup> Decreased renal perfusion and glomerular filtration resulted in acute renal failure that nature. In preeclampsia there is damage to the anatomical structure of the kidney so that GFR and RBF decreased. Decline in glomerular filtration rate that resulted in reduced plasma volume plasma creatinine levels increased almost two times higher than normal levels during pregnancy because of the high reabsorption in the kidney.<sup>9</sup>

Preeclampsia-eclampsia and high maternal mortality rate in Indonesia is a phenomenon that can not be separated, as known three biggest causes of maternal mortality is preeclampsia-eclampsia, infection and bleeding after labor has lasted more than 30 years. As a referral center, the prevalence of eclampsia in Dr. Soetomo Hospital Surabaya is very high at 1.08%, compared to Bangkok (Siriraj Hospital) 0.2% and Singapore 0.12%. Indonesia as a developing country facing a major problem with the high prevalence of eclampsia compared to other ASEAN countries. In 2007, at Dr. Soetomo hospital obtained 46 eclampsia and 282 severe preeclampsia, and until now, preeclampsia and eclampsia is a leading cause of maternal death in Dr. Soetomo hospital.<sup>3</sup> It is associated with the identification of clinical conditions based on laboratory data by health worker so that treatment can be adequate.

The main goal of the preeclampsia treatment is to prevent seizures, prevent intracranial hemorrhage, prevent organ dysfunction and to deliver healthy baby. Preeclampsia-eclampsia is a major cause of maternal deaths that are difficult to prevent, unless the clinical condition of the mother with laboratory profiles can be identified quickly and well understood. Intracranial hemorrhage, pulmonary edema, heart failure, kidney failure and sepsis are some clinical conditions that can lead to maternal mortality. Laboratory profiles were identified through examination of leukocytes, platelets, AST, ALT, creatinine levels, and several others. An understanding of the condition of the mother is very important so that pregnancy can be terminated at the right time and get the appropriate treatment according to the complaints of the patient. This will contribute to efforts to reduce maternal mortality in preeclampsia-eclampsia.<sup>5</sup> This research aims to study the relationship between clinical and laboratory findings in preeclampsia-eclampsia patients who died in Dr. Soetomo hospital Surabaya.

## MATERIALS AND METHODS

This study was a retrospective observational analytic. The study population was all patients with preeclampsia-eclampsia that were treated in Dr. Soetomo hospital from January 2009 to December 2011. The variables include maternal conditions (pulmonary edema, cerebral edema, intracerebral hemorrhage, HELLP syndrome, DIC, renal failure and retinal detachment) and laboratory results (hemoglobin, leuko-cytes, hematocrit, platelets, GDA, AST, ALT, BUN, Creatinin, Na, K, albumin, LDH). Data retrieved from the medical records of Dr. Soetomo hospital Surabaya. Patients with preeclampsia-eclampsia diagnosis that meet the inclusion criteria included in this study, to assess the clinical and laboratory conditions and the outcome (alive or dead). The data were process-ed using SPSS software. In each of the variables tested in logistic regression.

## RESULTS

In this study, over a period of 3 years, from 1 January 2009 to 31 December 2011 found 247 cases with the diagnosis of preeclampsia-eclampsia found in the medical record. The number of maternal mortality rate is 26 cases (10.5 %).

Table 1. Characteristic of preeclampsia-eclampsia based on the clinical variables

Variables	n	%
HELLP Syndrome	65	26.3
Pulmonay edema	23	9.3
Cerebral edema	18	7.3
Acute Renal Failure	45	18.2
ICH	9	3.6

Table 2. Comparison of the HELLP Syndrome with AST, ALT, platelets count and LDH laboratory variables

Variable	B	P	R <sup>2</sup>
HELLP Syndrome	1.516	0.312	
AST >38	1.224	0.150	
ALT >40	2.216	0.001*	0.561
Thrombocytes <150000	3.581	0.0001*	
LDH >600	17.653	0.997	
Constanta	-5.869		

The incidence of HELLP Syndrome does not have a significant relationship with maternal mortality, but ALT >40 U/L (p = 0.001) and platelets count <150.000

/ $\mu$ L (p = 0.0001) had significant relationship with incidence of maternal mortality. Both of them played a role as predictor for maternal mortality in the HELLP Syndrome of 56.1% (R<sup>2</sup> = 0.561) (Table 2).

Table 3. Comparison of the ARF with BUN, creatinin and albumin laboratory variables

Variables	B	p	R <sup>2</sup>
ARF	-1.594	0.209	
BUN >20	0.475	0.422	
Creatinin >1.2	2.050	0.0001*	0.170
Albumin <3.5	-0.332	0.593	
Constanta	-2.839		

The incidence of Acute Renal Failure (ARF) did not have significant relationship to maternal death, but the creatinin serum >1.2 mg/dL (p = 0.0001) had significant relationship to maternal death and played a role as predictor for maternal death in Acute Renal Failure, with strength of prediction 17.0% (R<sup>2</sup>=0.170) (Table 3).

Table 4. Comparison of pulmonary edema with creatinin and albumin laboratory variables

Variable	B	p	R <sup>2</sup>
Pulmo edema	3.592	0.0001*	0.366
Creatinin >1,2	0.543	0.397	
Albumin <3,5	-0.304	0.651	
Constanta	-2.963		

Pulmonary edema had significant relationship to maternal mortality (p = 0.0001). The creatinin serum >1,2 mg/dL (p = 0.397) and albumin <3.5 g/dL (p = 0.651), which mean that the two variables did not have significant relationship to maternal mortality and both of them were not a predictor for maternal mortality with pulmonary edema. The prediction of the maternal death incident with pulmonary edema is 36.6% (R<sup>2</sup> = 0.366) (Table 4).

Table 5. Comparison of the cerebral edema with trombocytes laboratory variables

Variable	B	p	R <sup>2</sup>
Cerebral edema	1.764	0.003*	
Thrombocytes <150000	3.429	0.0001*	0.491
Constanta	-4.500		

The cerebral edema had a significant association with the incidence of maternal mortality (p = 0.003). Platelets count <150.000 / $\mu$ L also had a significant association with the incidence of maternal mortality (p = 0.0001). Platelets count <150.000/ $\mu$ L is a predictor for the

incidence of maternal death in cerebral edema with strength of prediction 49.1% ( $R^2 = 0.491$ ) (Tabel 5).

## DISCUSSION

From multivariate statistical tests of this study found no significant association between HELLP syndrome with the incidence of maternal mortality. This is consistent with reports of Ardian (2010) in his study in Dr. Soetomo hospital stating that there is no significant association between HELLP syndrome with the incidence of maternal mortality. This is in contrast to the findings of Sibai (1994) which states HELLP syndrome have a relationship with the incidence of maternal mortality, especially when it occurs after childbirth. Nevertheless, laboratory parameters, there are two variables:  $ALT > 40$  U/L and platelets count  $< 150.000$  / $\mu$ L having meaningful relationships as a predictor of the incidence of maternal mortality in HELLP syndrome. This means that clinically HELLP syndrome had no significant correlation with the incidence of maternal mortality, but an increase in  $ALT > 40$  U/L and a decrease in platelets count  $< 150.000$  / $\mu$ L would increase the incidence of maternal mortality in HELLP syndrome at 56.1%.

De Gracia (2009) reported that thrombocytopenia is a predictive factor maternal death of preeclampsia-eclampsia, but not explained on the presence or absence of HELLP syndrome. Muzayanah (2001) in his study stated that platelets below the threshold value will increase the risk of maternal death preeclampsia-eclampsia patients were significantly (platelets count =  $140.000$  / $\mu$ L).

Statistical analysis of this study found no significant relationship between the incidence of Acute Renal Failure with maternal mortality. These results are in contrast to reports of Sibai (1994) which states the incidence of Acute Renal Failure in preeclampsia-eclampsia was 7.7% and have a meaningful relationship with the mother's death. Khalid M (2004) stated that the incidence of Acute Renal Failure in the incidence of preeclampsia-eclampsia reached 25.8% and significantly associated with the incidence of maternal mortality. Creatinine serum  $> 1.2$  mg/dL had a significant association with the incidence of maternal mortality and is a predictor of the incidence of maternal mortality in Acute Renal Failure with a strong prediction of 17.0%. This means that although clinically Acute Renal Failure does not have a significant association with the incidence of maternal mortality, but an increase in serum creatinine  $> 1.2$  mg/dL will increase the incidence of maternal mortality in Acute Renal Failure.

In this study found 15 cases (65.2%) deaths with pulmonary edema. And found a statistically significant relationship between the incidence of pulmonary edema with maternal mortality. These results are consistent with reports of Sibai (2005) which states the incidence of pulmonary edema in preeclampsia-eclampsia by 2.9% and have a relationship with the incidence of maternal mortality.

From multivariate statistical tests of this study found a significant relationship between the incidence of pulmonary edema maternal mortality. Creatinine serum  $> 1.2$  mg/dL, and albumin  $< 3.5$  g/dL had no statistically significant association with the incidence of maternal mortality in pulmonary edema. This means that clinical pulmonary edema had a significant association with the incidence of maternal mortality, but creatinine serum  $> 1.2$  mg/dL and albumin  $< 3.5$  g/dL is not a predictor for the incidence of maternal mortality in pulmonary edema. Pulmonary edema will increase the incidence of maternal mortality by 36.6%.

It is clear that the laboratory parameters did not affect the incidence of pulmonary edema maternal preeclampsia-eclampsia patients. Bachelor Dildy and Belfort (2007) also stated that the occurrence of pulmonary edema are closely related to excess fluid therapy given during the treatment. Dildy and Belfort (2007) also states that an overly aggressive fluid administration during labor patients with preeclampsia-eclampsia increases the risk of pulmonary edema. Edema can also be caused by aspiration pneumonitis occurring after inhalation of gastric contents in case of seizure accompanied by vomiting.

Statistical analysis there were significant relationship was found between the incidence of cerebral edema and maternal mortality, as well as platelets count  $< 150.000$  / $\mu$ L also had significant association with the incidence of maternal mortality. This means that clinical cerebral edema have a significant association with the incidence of maternal mortality. The platelets count  $< 150.000$  / $\mu$ L is a predictor for the incidence of maternal death in cerebral edema with a strong prediction of 49.1%.

Presence of thrombocytopenia in cerebral edema is still overlapping with thrombocytopenia in the incidence of ICH. It is difficult to insure the cause of death thrombocytopenia induced cerebral edema or ICH without other complications such as HELLP syndrome. Routine evaluation by scanning or imaging is needed.<sup>8</sup> It is clear that the findings of cerebral edema in patients with preeclampsia-eclampsia were obtained by CT scans, rare retrieval for evaluation of worsening of the disease. In addition, at the Dr. Soetomo Hospital never performed

brain surgery on a patient examination of the suspect died from cerebral edema or ICH.

In this study, there is 9 cases (100%) deaths due to ICH. This figure is much higher than the findings of scholars Park (2007) which states that 15-20% of deaths from preeclampsia-eclampsia due to intracerebral hemorrhage. According to the statistical test found a significant association between the incidence of ICH with maternal mortality. This is consistent with studies conducted by scholars BT Bateman et al stated that ICH caused by preeclampsia-eclampsia is substantially related to the incidence of maternal mortality. Simolke GA (1991) declared the death of the patient due to ICH eclampsia by 20% and have a meaningful relationship with the maternal mortality. Isler CM et al (1999) stated that the cause of maternal death with HELLP syndrome is most often intracerebral hemorrhage (26.4%). Miguil (2008) also states that the brain hemorrhage is the leading cause of death in eclampsia, in addition to multi-organ failure.

## CONCLUSION

Clinical profiles in preeclampsia-eclampsia patients who died in Dr. Soetomo Hospital, Surabaya, have correlation with their laboratory profiles.

## REFERENCES

1. Chhabra S and Kakani A. Maternal Mortality due to Eclamptic and Non Eclamptic Hypertensive disorders : a challenge, *Journal Obstetry and Gynecology*. 2007; 27(1) : 25-9
2. Cunningham GF, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC and Wenstorm KD. Hypertensive Disorder in Pregnancy. in *William Obstetric* 23rd Edition. 2010; 764-78
3. Dachlan EG. Karakteristik Pre Eklampsia-Eklampsia Indonesia Sebagai Penyebab Utama Kematian Ibu Bersalin. *Fakultas Kedokteran Universitas Airlangga, Airlangga University Press AUP*. 2008; 2-11
4. Mackay AP, Berg CJ and Atrash HK. Pregnancy-Related Mortality from Preeclampsia and Eclampsia, *The American College of Obstetricians and Gynecologists*. 2001; 97: 533-8.
5. Muzayannah. Penilaian Hasil Laboratorium Sebagai Faktor Prognosis Kematian Maternal Pada Preeklampsia-Eklampsia, *Bagian Obgin RSUP Dr. Sardjito/FK UNDIP, Jogjakarta*: 2002.
6. Park, Belfort and Norwitz ER. Pathogenesis and treatment of eclampsia, *Pre Eclampsia etiology and clinical practice*, Cambridge University Press. 2007; 437-47
7. Sherman RW, Bowi RA, Henfrey MME, Mahajan RP and Bogod D. Cerebral Haemodynamics in Pregnancy and Preeclampsia as Assessed by TransCranial Doppler Ultrasonography, *British Journal of Anaesthesia*. 2002; 89(5): 687-92
8. Simolke GA, Susan M and Cunningham FG. Cerebrovascular Accident Complicating Pregnancy and the Puerperium, *University Southwestern Medical Center of Dallas, Texas*. 1991; 78: 37-42
9. Smith MC and Davison JM. 2007. The Kidney and Preeclampsia, In : *Pre-eclampsia Etiology and Clinical Practice*, Cambridge University Press, New York, 23: 339-355
10. Suarez B, Alves K, Senat MV, Fromageot J and Fischer C. Abdominal Pain and Preeclampsia, *The American Institute of Ultrasound in Medicine*. 2002; 21: 1077-1083
11. Varner M. The Differential diagnosis of preeclampsia and eclampsia, In : *Pre-eclampsia Etiology and Clinical Practice*, Cambridge University Press, New York: 2007; 26: 380-405