Research Article

Factors Influencing Maternal Mortality from Severe Preeclampsia and Eclampsia

Faktor-faktor yang Mempengaruhi Kematian Ibu pada Preeklampsia Berat dan Eklampsia

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Abstract

Objective: To analyze risk factor, both clinical and laboratory findings, associated with maternal mortality from severe preeclampsia and eclampsia in Atma Jaya Hospital.

Methods: This was a retrospective case control study. All medical records of maternal death associated with severe preeclampsia and eclampsia between 1st January 2009 and 31st December 2011 were obtained and then information about risk factors were collected and tabulated. Risk factor analyzed were maternal age, gestational age, parity, coexisting medical illness (hypertension), antenatal examination status, maternal complications, systolic and diastolic blood pressure at admission, and admission laboratory data.

Results: There were 19 maternal deaths associated with severe preeclampsia and eclampsia during period of study (Consisted of 6 cases of eclampsia and 13 cases of severe preeclampsia). Maternal mortality rate for severe preeclampsia and eclampsia were 16.7% and 33.3% respectively. Multivariate analysis identified the following risk factors associated with maternal death: gestation age <32 week, history of hypertension, thrombocyte count < 100.0000/µl, post partum bleeding, acute pulmonary edema, HELLP syndrome, and sepsis.

Conclusion: In this study, we found that gestational age, history of hypertension, and platelet count are the cause of maternal mortality. Maternal complications associated with maternal mortality are post partum bleeding, acute pulmonary edema, HELLP syndrome, and sepsis.

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Keywords: eclampsia, maternal mortality, preeclampsia,

Abstrak

***Tujuan**: Untuk menganalisis faktor-faktor risiko (klinis dan temuan laboratorium) yang berhubungan dengan kematian ibu akibat preeklampsia berat dan eklampsia di Rumah Sakit Atma Jaya.*

***Metode**: Penelitian ini merupakan studi kasus kontrol. Semua catatan medis kematian ibu akibat preeklampsia berat dan eklampsia antara tanggal 1 Januari 2009 dan 31 Desember 2011, diperoleh informasi tentang faktor risiko kematian kemudian dikumpulkan dan ditabulasi. Faktor risiko yang dianalisis adalah usia ibu, usia kehamilan, paritas, riwayat penyakit (hipertensi), status kehamilan, komplikasi ibu, tekanan darah sistolik dan diastolik saat masuk, dan data hasil laboratorium.*

***Hasil**: Terdapat 19 kasus kematian ibu akibat preeklampsia berat dan eklampsia selama waktu penelitian, yang terdiri dari 6 kasus eklampsia dan 13 kasus preeklampsia berat. Angka kematian ibu untuk preeklampsia berat dan eklampsia adalah 16,7% dan 33,3%. Analisis multivariat menunjukkan faktor-faktor risiko berikut terkait dengan kematian ibu: usia gestasi <32 minggu, riwayat hipertensi, jumlah trombosit <100.0000/µl, perdarahan post partum, edema paru akut, sindrom HELLP, dan sepsis.*

***Kesimpulan**: Dalam penelitian ini, kami menemukan bahwa usia kehamilan, riwayat hipertensi,dan jumlah trombosit merupakan penyebab kematian ibu. Komplikasi ibu terkait dengan kematian ibu adalah perdarahan post partum, edema paru akut, sindrom HELLP, dan sepsis.*

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***Kata kunci**: eklampsia, kematian ibu, preeklampsia*

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INTRODUCTION

Preeclampsia is a pregnancy-related hypertensive disorder which usually occurs after 20 weeks of gestation. If left untreated, it will progress to eclampsia.[1] Preeclampsia and eclampsia are not distinct disorders but are the manifestation of the spectrum of clinical symptoms of the same condition. The mildest disorder in this continuum is pregnancy-induced hypertension. In preeclampsia, hypertension and proteinuria are present, and when convulsions occur in addition to these signs, the condition is referred to as eclampsia.[2]

Hypertension in pregnancy, the majority of preeclampsia and eclampsia, are the leading causes of maternal mortality and morbidity in developing countries.[3,4] Preeclampsia and eclampsia are the major common complication of pregnancy, while others are bleeding and infection.[5] Globally, pre-

eclampsia and eclampsia account for 10%-15% of maternal deaths. The majority of deaths in developing countries result from eclampsia, while in developed countries, complications of pre-eclampsia are more often as a cause.[6] In the US, preeclampsia and eclampsia are the third leading cause of maternal mortality, accounting for 54 of 540 maternal deaths in 2004, followed by embolism and hemorrhage.[7] It can also lead to significant fetal morbidity and mortality, including an increased incidence of placental abruption, fetal growth restriction, and preterm delivery. Due to its frequent occurrence and potential severity, early diagnosis and appropriate management are essential.

Maternal mortality due to preeclampsia and eclampsia are caused by disseminated intravascular coagulation, acute renal failure, hepatocellular damage, hepatic rupture, intracerebral hemorrhage, cardiac arrest, respiratory failure, pulmonary edema, and hemorrhage after childbirth.[8]

METHODS

Data were derived from Atma Jaya Hospital. The data comprised of all patients with severe preeclampsia and eclampsia who were treated at Atma Jaya Hospital from 1 January 2009 until 31 December 2011.

This study was a case-control study, comparing the clinical parameters and laboratory between severe preeclampsia and eclampsia patients ended with death, and severe preeclampsia and eclampsia patients which did not end with death. The cases were all patients with severe preeclampsia and eclampsia who ended up died. Cases where the patient was already dead upon admittance to hospital were excluded. Whereas for the control, the samples taken were severe preeclampsia and eclampsia cases that occurred during the same year, but did not end with death.

The characteristics of subjects recorded in this study were age, gestational age, multiple pregnancies, primiparous, history of hypertension, antenatal examination, sopor-coma state. Age were classified into 2 groups, which is less than 35 years and more than 35 years, tailored to the research by Mackay and his colleagues which showed that maternal age over 35 years is associated with increased risk of death.[9] Based on gestational age, the subjects were classified into 2 groups: under 32 weeks and over 32 weeks. Previous studies mentioned that the gestational age below 32 weeks is a risk factor for maternal mortality.[10] Other risk factors such as primiparous, history of hypertension, poor antenatal examination and the state of coma sopor are risk factors for maternal mortality.[11] In addition to the characteristics, we also assessed the parameters of laboratory results. The laboratory results were classified into leukocytes, thrombocytes, SGOT, SGPT, and creatinine. Leukocytes were assessed with 15.000/μl threshold, platelets 100,000/μl threshold, AST and ALT 150 IU/l threshold, and creatinine 1.5 mg/dl threshold. Those values were used based on National High Blood Pressure Education Program report that said the value was associated with maternal mortality.[12]

Researches data obtained were recorded in a special form provided, then tabulated and analyzed with SPSS (Statistic Package for Social Science) computer software version 16 for Windows. Bivariate relationship between the studied risk factors and maternal mortality were tested using Chi square test for categorical data and Student t test for numerical data, as well as by calculating odd ratios and 95% confidence interval.

RESULTS

According to the data recorded between the years 2009-2011 in Atma Jaya Hospital, there were 1236 labor. As a whole, there were 96 recorded cases (7.8%) of preeclampsia and eclampsia, in which there were 18 cases (1.5%) of eclampsia. Hence, on average year there are 24 severe preeclampsia patients and 6 eclampsia patients. Between the years of 2009-2011 there were 32 recorded cases of maternal mortality and 19 (59.4%) of them occurred in patients with severe preeclampsia and eclampsia.

Between the years 2009-2011 there were 19 maternal deaths associated with severe preeclampsia or eclampsia. 6 cases (31.6%) were eclampsia, and the rest were cases of severe preeclampsia, so the percentage of deaths due to eclampsia was 33.3% and for severe preeclampsia was 16.7%.

47.4% of patients were referred by an obstetrician and gynecologist, while the rest were referred by midwife, general practitioner or came without referral. Age of the patients who died ranged between 20 years to 39 years, the average was 28.2 years. A total of 6 patients (31.6%) were primi-

parous. 26,3% patients were doing antenatal examination during pregnancy and 47.4% of whom were examined by midwife.

In the case, 11 patients (57.9%) were not in labor yet. In 5 of 6 cases of eclampsia (83.3%), seizures occurred before or during birth. Most of the seizures occurred before the patient entered the Atma Jaya Hospital, but there was 1 case in which the first seizure occurred at Atma Jaya Hospital. In 4 of 6 cases of eclampsia (66.6%) patients were admitted to hospital with sopor or coma level of consciousness, while the other two were in a circulatory shock condition. The major causes of death were bleeding and respiratory failure caused by pulmonary edema, sepsis, and HELLP syndrome.

Patients with severe preeclampsia and eclampsia in Atma Jaya Hospital died after averagely 5.3 days of treatment. A total 5 (26.3%) patients died within the first 24 hours and 31.6% of patients died after undergoing treatment for 7 days. The patient being treated the longest was the one who had severe preeclampsia with pulmonary edema. The patient were treated up to 18 days before finally died from septic shock. About 57.9% died in the intensive care unit, while the rest died in the delivery room or on the operating table.

As a control, we obtained 77 patients consisting of 12 eclampsia patients and 65 severe pre-eclampsia patients. Clinical comparison between case patients and control patients can be seen in Table 1.

Table 1. Patient characteristics of case patients and control patients

Characteristics	Case (n=19)		Control (n=77)		p
		SD (%)		SD (%)	
Mean age (year)	28.2	6.5	29.6	7.50	0.439
Age >35 year	3	15.80	19	24.70	0.311
Gestation age <32 weeks	9	47.40	5	6.50	0.000*
Multiple Pregnancy	2	10.50	3	3.90	0.256
Primiparous	13	68.40	52	67.50	0.568
History of hypertension	10	52.60	13	16.90	0.002*
Antenatal examination	4	21.10	17	22.10	0.597
A state of sopor-coma	2	10.50	5	6.50	0.420
Systolic	176 mmHg	SD=16.7	170.5 mmHg	SD=17.8	0.203
Diastolic	110 mmHg	SD=14.3	106 mmHg	SD=12	0.197

SD=Standard Deviation
**= significant*

The patient was examined for blood pressure measurements at the Atma Jaya Hospital, before being given anti hypertensives. Anti hypertensive medication consumed before may affect the value obtained.

Any patient with a diagnosis of severe preeclampsia or eclampsia who entered the Atma Jaya Hospital was generally had their blood samples taken directly for laboratory examination. Initial laboratory data of patients admitted to Atma Jaya Hospital can be seen in Table 2. For multivariate analysis, significant laboratory value is classified into 2 groups (Table 3).

Table 2. Initial laboratory data of patients admitted to Atma Jaya Hospital

Variable	Mean Case	SD	Mean Control	SD	p
Proteinuria (semi-quantitative)	2.4	10.6	2.3	0.9	0.59
Haemoglobin (gr/dl)	11.5	1.9	11.6	1.6	0.79
Haematokrit (vol%)	36.2	5.9	36.4	3.9	0.79
Leucocyte (/µl)	16.258	4.107	13.982	4.465	0.04*
Thrombocyte (/µl)	197.584	133.624	244.497	90.321	0.07
SGOT (IU/l)	147	170	115	100	0.29
SGPT (IU/l)	124	129	99	94	0.34
Creatinine (mg/dl)	1.3	0.6	1.2	0,5	0.72

SD=Standard Deviation
**= significant*

Table 3. Laboratory parameter comparison between case patients and control patients

Variable	Case		Control		p	OR	CI 95%
	n	%	n	%			
Leukocyte							
> 15.000/µl	13	68.40%	34	44.20%	0.075	0.4	0.18-1.07
<15.000/µl	6	31.60%	43	55.80%			
Thrombocyte							
<100.000/µl	8	42.10%	8	10%	0.003*	3.6	1.74-7.59
>100.000/µl	11	57.90%	69	90%			
SGOT							
>150 IU/l	11	57.90%	34	44.20%	0.314	0.6	0.28-1.45
<150 IU/l	8	42.10%	43	55.80%			
SGPT							
>150 IU/l	8	42.10%	31	40.30%	1	0.9	0.42-2.12
<150 IU/l	11	57.90%	46	59.70%			
Creatinine							
>1,5 mg/dl	10	52.60%	35	45.50%	0.616	0.8	0.36-1.78
<1,5 mg/dl	9	47.40%	42	54.50%			

**=significant*

Complications explained here include the complications that had occurred when patients came in as well as other complications that aroused during treatment. These complications may be due to complications of preeclampsia such as HELLP syndrome, pulmonary edema, or other complications such as post-partum bleeding, magnesium sulfate intoxication, sepsis, and vagal reflexes. Comparison

of complications that occured in mothers between cases and controls can be seen in Table 4.

Table 4. Comparison of maternal complications

Variable	Case	%	Control	%	p
Post partum bleeding	10/19	52.60%	4/77	5.20%	0.000*
Acute pulmonary edema	11/19	57.90%	7/77	9.10%	0.000*
HELLP syndrome	8/19	42.10%	7/77	9.10%	0.002*
Sepsis	9/19	47.40%	5/77	6.50%	0.000*

**=meaningful*

DISCUSSION

Although the number of patients who died from severe preeclampsia was higher than eclampsia patient, but the death rate of eclampsia is much higher, reaching to 33.3%, compared with severe preeclampsia 16.7% (from 2009-2011). This figure is much higher than compared with developed countries, where the death rate from eclampsia reach 0.4%.[9]

This study was primarily aimed to determine what factors are associated with the occurrence of death in patients with severe preeclampsia and eclampsia. From univariate analysis, factors found associated with the occurrence of maternal deaths were gestational age, a history of hypertension, thrombocyte <100,000/µl. Maternal complications found related to death are post partum bleeding, pulmonary edema, HELLP syndrome, and sepsis.

Age differences between cases and controls were found not statistically significant. When classified into 2 groups (less than 35 years and over or equal to 35 years), there was still no significant difference found. This is probably caused by the number of patients with relatively a few cases, so it did not give significant differences.[1]

The characteristic based on gestational age was classified into 2 groups: under 32 weeks and over 32 weeks. Previous studies mentioned that the gestational age below 32 weeks is a risk factor for maternal mortality.[10] The above research shows that gestational age less than 32 weeks has an important role in maternal mortality. Morbidity and mortality number of preeclampsia and eclampsia occurring in preterm pregnancies were occasionally higher than those in term pregnancies. This fact is important to note, especially if we're going to conservatively manage patients with severe preeclampsia at less than 32 weeks gestation.

Repeated labor will give a lot of risk to the pregnancy. In addition, one theory that predisposes to severe preeclampsia and eclampsia is the factor of parity (primigravida). Statistical record shows that from worldwide incidence, from 5%-8% of all preeclamptic pregnancies, more than 12% of them were primigravida.[13] Factors affecting the frequency of primigravida preeclampsia are found more frequently than in multigravida, especially the young primigravida.[14] From our research, it was found that those two factors do not play an important role in the deaths of hospital patients in our study.

A history of chronic hypertension may aggravate the complications of severe preeclampsia and eclampsia because sometimes there are also a kidney disorder, heart muscle disorders, as well as a higher risk of stroke. Early detection and counseling for pregnant patients with a history of chronic hypertension is very important.[8,11] From the statistical research conducted by us, it was found that a history of hypertension had a role in maternal mortality.

Antenatal examination also seemed unrelated to risk of death. But the quality of antenatal examination was not inspected in this study. Some research suggests mothers not to do antenatal examination, at risk of experiencing a complicated eclampsia and death from preeclampsia and eclampsia.[15] This finding may reflect a poor quality of antenatal care that any symptoms or signs of complication of a pregnancy are not detected or not handled properly. In addition, information about the symptoms or signs of danger in pregnancy, may be not understood by patients, so in some cases, patients are too late to seek help from a midwife or a doctor, even if the symptoms are present long enough to be felt.[11]

Apart from that, the state of sopor-coma in our study did not show the causes of death although the actual state of sopor-coma may aggravate severe preeclampsia and eclampsia.

In this study, we obtained several laboratory parameters associated with the risk of maternal death, such as thrombocyte. This is consistent with the incidence of complications of HELLP syndrome in a patient who died. Approximately 50% of patients with HELLP syndrome are also accompanied by other complications such as eclampsia, sepsis, and DIC.

Leukocyte count in the case group was found to be significantly higher than in the control group (16.258 SD 4.107/μl vs 13.982 SD 4.465, p=0.04). The results are statistically significant but not clinically significant. Higher leukocytes may be caused by infection or sepsis is more common in the case. Leukocytes of patients presenting over 15,000 in the case is 68.4% compared with 44.2% of control.

Other parameters associated with the risk of maternal death are SGOT, SGPT, and creatinine. Increase in SGOT, SGPT, and creatinine showed that most patients who died had a kidney and liver complications. But in this study, these parameters did not show significant thing. This is probably caused by the number of patients with relatively a few cases, so it did not give significant differences.

In this study, it was found that 10 of 19 patients who died, or about 52.6%, had bleeding complications. And it was found that 9 of 19 patients who died, or about 47.4%, had sepsis complications.

Acute pulmonary edema was also seen as one cause of death. Pulmonary edema can occur after seizures of eclampsia. This can occur due to pneumonia from aspiration of gastric contents into the respiratory tract caused by vomiting during the seizure. Moreover, it can also due to cardiac decompensation experienced by patients, as a result of severe hypertension and excessive fluid administration.[11,16]

Apart from clinical factors and obstetric complications above, the factors of health services also have a very large role in maternal mortality. These factors include the difficulty of access to maternal health services, poor medical care, and inadequate or unaffordable support facilities. By analyzing these factors, precautionary measures to reduce maternal mortality can be carried out.[17]

CONCLUSION

Factors associated with maternal mortality was gestation age below 32 weeks, with a history of hypertension, laboratory results below 100,000/μl, had some maternal complications such as post partum bleeding, acute pulmonary edema, HELLP syndrome, and sepsis. The goal of this study is to find out the cause of death of preeclampsia and eclampsia patients, so mortality can be anticipated and be reduced.

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