Clinical Research

Determinants of low APGAR score among preeclamptic deliveries in Cipto Mangunkusumo Hospital: a retrospective cohort study in 2014

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ABSTRAK

Latar belakang: *Preeklampsia berimplikasi besar pada luaran neonatus. Skor* appearance, pulse, grimace, activity, respiration *(APGAR) 1 atau 5 menit adalah salah satu indikator kematangan fisiologis anak. Oleh karena itu, penelitian ini bertujuan mencari hubungan skor APGAR pada persalinan dengan preeklampsia.*

Metode: *Penelitian ini menggunakan design kohort retrospektif. Data didapatkan pada bulan Januari sampai Desember 2013 dari seluruh wanita preeklamsia yang melahirkan bayi tunggal di Rumah Sakit Cipto Mangunkusumo, Jakarta. Hasil luaran salah satunya berupa skor APGAR. Analisis multivariat dengan menggunakan binari logistik digunakan untuk mencari korelasi antara skor APGAR dengan faktor-faktor resiko pada preeklampsia, hasil penelitian diuji dengan uji kai kuadrat.*

Hasil: *Sebanyak 446 memenuhi kriteria inklusi dari 450 wanita dengan preeklampsia, 4 diantaranya tereksklusi karena data yang tidak lengkap. Skor APGAR 1 dan 5 menit berhasil dikumpulkan pada 19% (86/446) dan 5,4% (24/446) dari neonatus. Onset awal preeklampsia (OR adj = 4,577; 95% CI = 2,147 – 9,757), leukosit darah ≥ 15.000/µL (OR adj = 3,315; 95% CI = 1,738 – 6,324), sindrom HELLP (OR adj = 2,00; 95% CI = 1,38–2,91) merupakan faktor risiko independen pada skor APGAR rendah 1 menit pertama. Sementara itu, tidak terdapat faktor risiko yang signifkan antara determinan dengan skor APGAR 5 menit pertama.*

Kesimpulan: *Leukositosis, onset awal preeklampsia, lahir* preterm*, trombositopenia, derajat preeklampsia, dan sindrom HELLP adalah faktor risiko independen skor APGAR rendah dalam satu menit pada anak yang lahir dari ibu dengan preeklampsia.*

ABSTRACT

Background: Preeclampsia has great implication on adverse neonatal outcome. Appearance, pulse, grimace, activity, respiration (APGAR) score at 1 or 5 minutes is one of the indicators of physiologic maturity of the infant. Therefore, the aim of this study was to know the correlation of APGAR score in preeclamptic deliveries with its risk factors.

Methods: This study was a retrospective cohort. Data were collected from January to December 2013 including all preeclamptic women with singleton live pregnancies who delivered their babies in Cipto Mangunkusumo Hospital, Jakarta. The primary outcome was APGAR score. There were some determinants conducted in this study. Binary logistic was used as multivariate analysis to analyze the correlation between APGAR score and risk factors of preeclampsia, data were analyzed using chi square test.

Results: Out of 450 preeclamptic women, 446 of them met the inclusion criteria. Low APGAR scores at 1 and 5 minutes were found in 19% (86/446) and 5.4% (24/446) of neonates respectively. Early onset of preeclampsia (adjusted OR = 4.577; 95% CI = 2.147 - 9.757), white blood cell ≥ 15,000/µL (adjusted OR = 3.315; 95% CI = 1.738 – 6.324), HELLP syndrome (adjusted OR = 2.00; 95% CI = 1.38 – 2.91) were independent risk factors for having infant with low APGAR score at 1 minute. Meanwhile, there was no significant risk factors at 5 minutes APGAR score after adjustment.

Conclusion: Leukocytosis, early onset preeclampsia, preterm birth, and thrombocytopenia, severity of preeclampsia, and HELLP syndrome are independent risks of having infant born with low APGAR score at 1 minute in preeclamptic deliveries.

Keywords: APGAR score, newborn, preeclampsia

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Preeclampsia is one of the common conditions of unknown etiology which increase the risk of maternal and perinatal morbidity and mortality.[1] The exact etiology of preeclampsia remains unknown. Factors that are currently more accepted include abnormal trophoblast invasion of uterine blood vessels, increased vasopressor response and vasospasm, immunological intolerance to the fetus and genetic abnormalities.[2] Preeclampsia affects three to five percents of pregnancies, it is an important factor in fetal growth restriction as it is commonly associated with placental insufficiency.[3] Preeclampsia is a complex, pregnancy – specific hypertensive syndrome of reduced organ perfusion related to vasospasm and activation of the coagulation cascade affecting multiple systems. The major risk to the fetus results from decreased placental perfusion leading to decreased blood supply of oxygen and nutrients necessary for fetal growth and wellbeing.[1,3]

The various complication seen are low appearance, pulse, grimace, activity, respiration (APGAR) score, intra-uterine growth restriction (IUGR), low birth weight, and increased need for admission to neonatal intensive care unit (NICU).[4,5]

The APGAR score, devised in 1952 by Dr. Virginia Apgar, is a quick method of assessing the clinical status of the newborn infant.[6,] The APGAR score comprises of five components: heart rate, respiratory effort, muscle tone, reflex irritability, and color, each of which is given a score of zero, one, or two.[6] It is important to recognize that elements of the APGAR score are partially dependent on the physiologic maturity of the infant. Low APGAR scores may be indicative of a number of maternal and infant factors.[6] Identification of possible intrauterine causes of low APGAR score may be important for the prevention of conditions that have been linked to low APGAR score at birth.[7,8]

Some studies found that preeclamptic women tend to have infant with low APGAR score than healthy women.[9,10] Proteinuria and increased blood pressure in preeclampsia are associated with a lower fetal birth weight and a lower APGAR score and an increased risk of adverse perinatal outcome.[11-13] Gawde, et al found that in severe cases of preeclampsia, the APGAR score at one minute is two-fold worse than in mild preeclampsia.[1] Five minutes APGAR score also associated with several obstetric risk factors and used to predict the effectiveness of resuscitation.

Preeclampsia is frequently seen in Indonesian population. The intended use of APGAR score has always been the same: to evaluate a newborn's condition at birth. This study was conducted to correlate preeclampsia with APGAR score to asses the condition of newborn infant.

METHODS

This retrospective cohort study was performed between January to December 2013. The inclusion criteria were preeclamptic women with singleton live pregnancy who delivered their babies in Cipto Mangunkusumo Hospital, Jakarta. The exclusion criteria were patients with incomplete data. The study population consisted of 450 preeclamptic women, four out of them were excluded for not having a complete data. Primary outcome measure was morbidity of the infant as in APGAR score at first and fifth minutes which were determined by perinatology residents. We divided group of low APGAR score (< 7) and normal APGAR score (≥ 7). We obtained data from the database based on medical record, which included age of gestation, maternal age, IUGR, eclampsia, anemia, low birth weight, mean arterial pressure (MAP), early or late preeclampsia, parity, white blood cell, platelet, frequency of antenatal care (ANC), and severity of preeclampsia which we used as independent variables.

Gestational age was calculated as the best obstetrical estimate according to the last menstrual period, or if it is not available, we used ultrasonography. IUGR was diagnosed based on ultrasonography when the fetal weight is less than the tenth percentile for the gestational age, or at least two standard deviations below the mean weight for the gestational age. Diagnosis for mild preeclampsia was based on systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on two occasions, proteinuria ≥ 300 mg per 24 hours or positive (+) using dipstick test but without evidence of end organ damage in the patient; severe pre-eclampsia if the systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg measured at least twice in several minutes, proteinuria > 5 g per 24

hours collection or ≥++ dipstick test on two random urine samples or symptoms, and or biochemical and or hematological impairment, and any organ involvement. Hemolysis, elevated liver enzyme levels, low platelet levels (HELLP) syndrome was defined as preeclampsia with platelet count persistently <100,000/mm^3, serum transaminases twice than normal. Superimposed pre-eclampsia was women with chronic hypertension and *de novo* proteinuria after 20 weeks of pregnancy. Early or late preeclampsia were defined as mothers who diagnosed preeclampsia either at <34 weeks or ≥34 weeks of gestational age.

Binary logistic was used as multivariate analysis to analyze the correlation between age of gestation, maternal age, IUGR, eclampsia, anemia, low birth weight, MAP, early or late preeclampsia, parity, leukocyte, platelet, frequency of ANC, and severity of preeclampsia and APGAR score. P <0.05 was taken as the limit of statistical significance.

RESULTS

There were 2,143 deliveries registered in our database over a year period. Out of 450 women who were diagnosed as pre-eclampsia, 446 of them met the inclusion criteria and had a complete data. The distribution of characteristics and the risk factors of low APGAR score among the subjects are shown in table 1.

Table 2 shows the comparison of low APGAR score and normal score in one minute with risk factors of preeclampsia. We found that weeks of gestational age (WGA), platelet, hematocrit, white blood cell, onset of preeclampsia, IUGR, and MAP are statistically significant in this study. Maternal age, anemia, frequent ANC were not associated with preeclamptic women having infant with low APGAR score. We determined the cut off value of hematocrit count using receiver operating characteristics (ROC) curve. The cut-off levels for hematocrit was 38.95 %.

Table 3 shows the comparison of low APGAR score and normal score in five minutes with confounding factors of preeclampsia. We found that WGA, platelet, onset and severity of preeclampsia were statistically significant in this study. Maternal age, anemia, white blood cell, hematocrit, frequent ANC, and MAP were

Table 1. Clinical characteristics and delivery outcomes of preeclamptic women in the study

Variables	Values
Maternal age (year), n (%)	
Low risk (< 35)	288 (64.7%)
High tisk (≥ 35)	157 (35.3%)
Parity, n (%)	
Nullipara	183 (41%)
Multipara	263 (59%)
WGA (weeks), median (min – max)	37 (25 – 42)
Aterm, n (%)	268 (60.1%)
Preterm,n (%)	178 (39.9%)
Birth weight (grams), mean ± SD	2560 ± 781.04
Systolic BP (mmHg), median (min – max)	160 (90-270)
Diastolic BP (mmHg), median (min – max)	100 (100-170)
Mean arterial pressure (mmHg) (mean + SD)	126.67 (106-160)
Platelet count (x10^3/µL), median (min – max)	248 (19.9-69.7)
Hemoglobin level (g/dL), median (min – max)	13 (8-17)
Leukocyte level (x10^3/µL), median (min – max)	13.55 (7.22-31.80)
Hematocrit (%), mean ± SD	37.40 ± 14.98
APGAR score 1 minute, n (%)	
Low	86 (19.3%)
Normal	360 (80.7%)
APGAR score 5 minute, n (%)	
Low	24 (5.4%)
Normal	422 (94.6%)
ANC >3 times, n (%)	
Yes	361 (80.9%)
No	85 (19.1%)
Severity, n (%)	
Mild pre-eclampsia	48 (10.8%)
Severe pre-eclampsia	345 (77.4%)
Superimposed pre-eclampsia	15 (3.4%)
HELLP syndrome	38 (8.5%)
Eclampsia	31 (7%)
Onset, n (%)	
Early onset	99 (22.2%)
Late onset	347 (77.8%)
Anemia (Hb < 11 g/dl), n (%)	58 (13.6%)
IUGR, n (%)	29 (6.5%)

WGA = weeks of gestational age; APGAR = appearance, pulse, grimace, activity, respiration; ANC = antenatal care; HELLP = hemolysis, elevated liver enzyme levels, low platelet levels; IUGR = intra-uterine growth restriction

Table 2. Comparison between low and normal APGAR score at 1 minute group based on obstetrical characteristics

Variables	Low APGAR score n (%)	Normal APGAR score n (%)	p	OR (CI = 95%)
Maternal Age				
Productive	59 (68.6%)	229 (63.8%)	0.401	1.24 (0.75-2.05)
Non-productive	27 (31.4%)	131 (36.2%)		
Week of gestation				
Aterm (>34 weeks)	17 (19.8%)	251 (69.7%)	< 0.001*	0.11 (0.06 – 0.19)
Preterm (28 – 34 weeks)	69 (80.2%)	109 (30.3%)		
Platelet				
≥151x10^3/μL	65 (75.6%)	342 (95%)	< 0.001*	6.14 (3.10 – 12.15)
<151x10^3/μL	21 (24.4%)	18 (5%)		
Anemia				
No	70 (81.4%)	282 (78.3%)	0.532	1.21 (0.67 – 2.20)
Yes	16 (18.6%)	78 (21.7%)		
Hematocrit				
≥38.9	40 (46.5%)	111 (30.8%)	0.006*	1.95 (1.20 – 3.15)
<38.9	46 (53.5%)	249 (69.2%)		
Leukocyte				
≥15 × 10^3/μL	49 (57%)	125 (34.7%)	< 0.001*	0.40 (0.25 – 0.65)
<15 × 10^3/μL	37 (43%)	235 (65.3%)		
Antenatal care (ANC)				
Yes	68 (79.1%)	293 (81.4%)	0.623	0.86 (0.48 – 1.55)
No	18 (20.9%)	67 (18.6%)		
Onset				
Early-onset	55 (64%)	44 (12.2%)	< 0.001*	12.7 (7.41 – 21.90)
Late-onset	31 (36%)	316 (87.8%)		
Intra-uterine growth restriction				
Yes	12 (14%)	17 (4.7%)	0.002*	3.27 (1.50 – 7.14)
No	74 (86%)	343 (95.3%)		
Mean arterial pressure (mmHg)				
<135	59 (68.6%)	300 (83.3%)	0.002*	0.44 (0.26 – 0.75)
≥135	27 (31.4%)	60 (16.7%)		
Severity				
Mild pre-eclampsia[a]	4 (4.7%)	44 (12.2%)	< 0.001*	2.00 (1.38 – 2.91)
Severe pre-eclampsia	54 (62.8%)	291 (80.8%)		
Superimposed	6 (7%)	9 (2.5%)		
HELLP Syndrome	22 (25.6%)	16 (4.4%)		

*Chi-Square, [a]p < 0.05 severity of preeclampsia are fused in analyses; HELLP = hemolysis, elevated liver enzyme levels, low platelet levels

not associated with preeclamptic women having infant with low APGAR score.

We adjusted leukocyte ≥15×10^3/μL, early or late onset preeclampsia, preterm birth, platelet ≥ 151x10^3/μL**,** MAP ≥135 mmHg, hematocrit ≥38.95 % with APGAR score at one minute outcome and found leukocyte ≥15×10^3/μL (adj usted OR = 3.63; 95% CI = 1.93 – 6.86), early or late preeclampsia (adj usted OR = 0.20; 95% CI = 0.09 – 0.42), preterm birth (adj usted OR = 0.32; 95% CI = 0.14 – 0.70), and platelet level (adj usted OR = 0.38; 95% CI = 0.17 – 0.86) as independent risk factors for having infant with low APGAR score at one minute. Using binary logistic, we found that mothers with MAP ≥135 (adj usted OR = 1.00; 95% CI = 0.51 – 2.0) hematocrit ≥38.95% (adj usted OR = 0.75; 95% CI = 0.42 – 1.34) were

Table 3. Comparison between low and normal APGAR score at 5 minutes group based on obstetrical characteristics

Variables	Low APGAR score n (%)	Normal APGAR score n (%)	P	OR (CI = 95%)
Maternal age				
Low risk	16 (66.7%)	273 (64.6%)	0.837	1.10 (0.46 – 2.62)
High risk	8 (33.3%)	149 (35.4%)		
Week of gestation				
Aterm	4 (16.7%)	264 (62.6%)	<0.001*	0.12 (0.04 – 0.36)
Preterm	20 (83.3%)	158 (37.4%)		
Platelet				
≥ 15 x 10^3/µL	16 (66.7%)	391 (92.7%)	<0.001*	6.31 (2.50 – 15.89)
< 15 x 10^3/µL	8 (33.3%)	31 (7.3%)		
Anemia				
No	20 (87%)	347 (86.3%)	0.931	0.95 (0.27 – 3.29)
Yes	3 (13%)	55 (13.7%)		
Hematocrit				
≥38.95	10 (41.7%)	141 (33.4%)	0.406	1.42 (0.62 – 3.29)
<38.95	14 (58.3%)	281 (66.6%)		
Leukocyte				
≥15 x 10^3/µL	13 (54.2%)	161 (38.2%)	0.118	0.52 (0.23 – 1.19)
<15 x 10^3/µL	11 (45.8%)	261 (61.8%)		
Antenatal care (ANC)				
Yes	20 (83.3%)	341 (80.8%)	0.759	1.19 (0.40 – 3.57)
No	4 (16.7%)	81 (19.2%)		
Onset				
Early-onset	17 (70.8%)	82 (19.4%)	<0.001*	0.10 (0.04 – 0.25)
Late-onset	7 (29.2%)	340 (80.6%)		
Intra-uterine growth restriction				
Yes	5 (20.8%)	24 (5.7%)	0.003*	4.36 (1.50 – 12.70)
No	19 (79.2%)	398 (94.3%)		
Mean arterial pressure				
<135	18 (75%)	341 (80.8%)	0.485	0.71 (0.27 – 1.85)
≥135	6 (25%)	81 (19.2%)		
Severity				
Mild pre-eclampsia[a]	0 (%)	48 (11.4%)	<0.001*	1.26 (1.06 – 1.51)
Severe pre-eclampsia[b]	14 (58.3%)	331 (78.4%)		
Superimposed[c]	1 (4.2%)	14 (3.3%)		
HELLP syndrome	9 (37.5%)	29 (6.9%)		

*Chi-Square, [a]p <0.05, severity of preeclampsia are combined in analyses (a,b,c); HELLP = hemolysis, elevated liver enzyme levels, low platelet levels

not at increased risk for having infant born with low APGAR score.

We adjusted early onset preeclampsia, preterm birth, platelet ≥ 151x10^3/µL, and IUGR with APGAR score at five minutes outcome and found that early or late preeclampsia (adj usted OR = 0.205; 95% CI = 0.06 – 0.76), preterm birth (adj usted OR = 0478; 95% CI = 0.10 – 2.22), platelet (adj usted OR = 0.402; 95% CI = 0.15 – 1.11), and IUGR (adj usted OR = 0.05; 95% CI = 0.93 – 1.00) were not significant risk factor for infant born with low APGAR score.

DISCUSSION

In women with preeclampsia, we often see that there is an insufficient placental circulation.

Table 4. Multivariate analysis of low APGAR score (1 minute), low APGAR score (5 minutes) and its risk factors

Variable	Low APGAR score 1 minute			Low APGAR score 5 minutes		
	p	adjOR	95% CI	p	adjOR	95% CI
Leukocyte ≥15 x 0^3/µL	<0.001	3.63	1.93 – 6.86	-	-	-
Early onset preeclampsia	<0.001	0.20	0.09 – 0.42	0.17	0.205	0.06 – 0.76
Preterm birth	0.004	0.32	0.14 – 0.70	0.346	0.478	0.10 – 2.22
Platelet ≥15 x 10^3/µL	0.002	0.38	0.17 – 0.86	0.079	0.402	0.15 – 1.11
Mean arterial pressure ≥135 mmHg	0.98	1.00	0.51 – 2.00	-	-	-
Hematocrit ≥38.95%	0.33	0.75	0.42 – 1.34	-	-	-
Intra-uterine growth restriction	0.25	0.59	0.24 – 1.45	0.05	0.305	0.93 – 1.00

The association between abnormal placentation and preeclampsia is well known and is thought to involve in trophoblast invasion of maternal spiral arteries.[14] Abnormal placentation results in inadequate uteroplacental blood flow that can lead to unsuccessful pregnancy outcomes. It is well known that low APGAR score most commonly results from uteroplacental insufficiency which is a later clinical manifestation of poor placentation and placental ischemia as may caused by preeclampsia. This may lead to the high risk of perinatal morbidity and mortality.[14] In women with preeclampsia, we tend to see some of abnormality findings in physical and laboratory examinations due to the changes of blood circulation which is related to severity of preeclampsia. The major finding in this study was to conclude which covariates increase the risk of preeclampsia resulting a low APGAR score in neonates. Surprisingly, mean arterial pressure (MAP) was not a significant factor for preeclamptic women having infant born with low APGAR score after adjusting with other significant factors (platelet ≥151x10^9/µL, early onset preeclampsia, preterm birth, leucocyte ≥15×10^3/µL) this result is contradictive to Aabidha, et al[13] who stated that hypertensive disorders of pregnancy increase the risk of low APGAR score for infant compared to control. Frequent ANC (visit ≥3) was also not associated with increased risk for preeclamptic mothers having baby with low APGAR score which is contradictive to Saito, et al[2] study which showed that expert obstetric management can prevent these problems in most off-springs of those women, provided they receive antenatal care and give obstetricians time to act. This was probably due to lack of management on antenatal care that was given to mothers when they were pregnant. Although there were several often general concordance between our findings and those of others, discrepancies might be explained by factors that were neither evaluated nor controlled in our study.

Weeks of gestation is a strong risk factor of adverse respiratory outcome that was part of scoring in APGAR, it was obviously documented in several studies[10] which concluded prematurity as an independent risk factor for perinatal adverse outcomes (OR = 43.9; p = 0.001).[10] In this study, we found that preterm birth associated with increased risk of low APGAR score at one minute but not in five minutes. White blood cell counts and low APGAR score could possibly be explained by fetal inflammatory response syndrome (FIRS) because maternal white blood cell count is one of the indicators of intrauterine infection and development of FIRS. Aabidha, et al[13] found that white blood cell level of 15,750/mm^3 was a significant mean level correlated with intra-amniotic infection. It was shown that the risk was three fold higher for having infant born with low APGAR score.[13] Hematocrit level was found statistically significant in increasing risk of infant born with low APGAR score by using multivariate analyses. Hematocrit was not significant compared to other confounding factors (p >0.05). In this study, low platelet count was significantly associated with one minute low APGAR score in neonates. This finding of worsening thrombocytopenia may represent inflammatory process that could possibly associated in neonatal outcomes, in this case, low APGAR score in infant born. Surprisingly, after using multivariate analyses, there were no significant factors correlated with low APGAR score at five minutes of infant born, this may be caused by good resuscitation performed by the residents who helped survival of the infants.

Our study offers several strengths, the high number of preeclamptic women allowed us to study the association between obstetric parameters with neonatal outcome. However, our study has also weakness due to its retrospective design because it has potential of missing data. As we directly reported the data after delivery, we attempted to minimize bias. It was managed by well-trained obstetric residents on duty and rechecked by the consultants.

In conclusion, our study found that some of abnormal laboratory findings, severity of preeclampsia and preterm birth lead to low APGAR score in neonates. Early management of preeclampsia is needed to improve the survival of neonates born. Patients need to be educated in recognizing the warning symptoms of preeclampsia before it develops and causes complications.

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Conflicts of Interest
The authors affirm no conflict of interest in this study.

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