JKKI : JURNAL KEDOKTERAN DAN KESEHATAN INDONESIA

UNIVERSITAS ISLAM INDONESIA
P-ISSN : 20854145 E-ISSN : 25272950 Subject Area : Health, Science

1.14286
Impact Factor

1603
Google Citations

Sinta 2
Current Acreditation

Google Scholar Garuda Website Editor URL

History Accreditation

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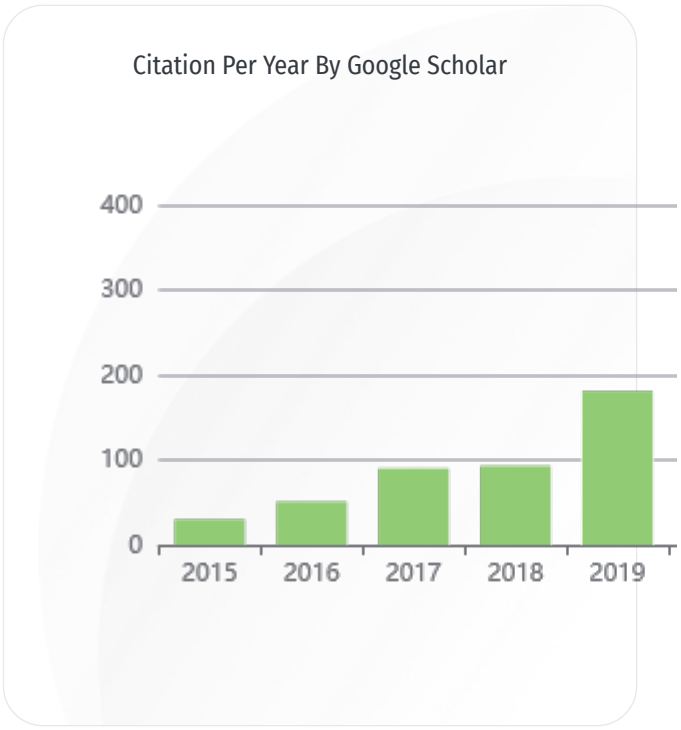

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Risks of preterm birth and low Apgar score among preeclamptic women

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Original Article

ARTICLE INFO

Keywords:
preeclampsia,
preterm birth,
Apgar score

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DOI: 10.20885/JKKI.Vol11.Iss1.art3

History:
Received: September 11, 2019
Accepted: February 11, 2020
Online: April 30, 2020

ABSTRACT

Background: Preeclampsia has been a major problem for obstetric care in Indonesia due to risks of preterm birth and lower Apgar score.
Objective: This study is to examine relationships of preeclampsia, preterm births, and Apgar Score.
Methods: This used an analytic study with retrospective case-control design in Dr. Soetomo Academic Hospital. A case group was taken by total sampling from medical records of all patients who had preterm delivery in 2017, and a control group of term deliveries was taken by random sampling. Then the data were analysed by using Chi-square test and Fisher's Exact Test.
Results: There were 80 samples for each group. 63.75% of patients by age of 20-35 years were who delivered preterm birth, 40.00% had normal BMI, 40.00% were nulliparous, 92.50% did not have history of preterm labour, 50.00% had preeclampsia with severe features, and 46.25% had spontaneous vaginal delivery. Around 47.14% neonates from preeclamptic women were born at 32-<37 weeks gestation, 50.00% were born with low birth weight, 52.86% had the first minute Apgar score <7, and 72.86% had the fifth minutes Apgar score ≥7. The statistical analysis showed a significant relationship between the preeclampsia and the preterm birth (p<0.007; OR=2.54, 95% CI 1.34-4.83). The preeclampsia was also related to lower Apgar score at 1st minute (p<0.042; OR=2.03, 95% CI 1.07-3.85) and 5th minute (p<0.046; OR=2.42, 95% CI 1.08-5.41). Preterm neonates born from preeclamptic mothers were related to lower Apgar score at 1st minute (p<0.002; OR=5.82, 95% CI 1.99-17.02) and 5th minute (p<0.001; OR 17.31, 95% CI 2.15-139.54).
Conclusion: Preeclampsia could make pregnant women at risks of delivering preterm birth and neonates with low Apgar score.

Latar Belakang: *Preeklampsia masih menjadi masalah utama dalam perawatan kebidanan di Indonesia karena risiko kelahiran prematur dan skor Apgar yang lebih rendah.*
Tujuan: *Untuk menganalisis hubungan preeklampsia, kelahiran prematur, dan Skor Apgar.*
Metode: *Penelitian analitik dengan desain kasus kontrol retrospektif di Rumah Sakit Umum Dr. Soetomo. Kelompok kasus diambil secara total sampling dari rekam medis semua pasien yang melahirkan prematur pada tahun 2017 dan kelompok kontrol diambil secara acak dari kelahiran aterm. Data dianalisis menggunakan uji Chi-square dan Fisher's Exact Test.*

Hasil: *Didapatkan 80 sampel untuk setiap kelompok. Pasien yang melahirkan prematur 63,75% berusia 20-35 tahun, 40,00% memiliki IMT normal, 40,00% nulipara, 92,50% tidak memiliki riwayat persalinan prematur, 50,00% mengalami preeklampsia berat, 46,25% melahirkan spontan. Sekitar 47,14% neonatus dari wanita preeklampsia dilahirkan pada usia kehamilan 32-<37 minggu, 50,00% dilahirkan dengan low birth weight, 52,86% memiliki skor Apgar menit pertama <7, dan 72,86% memiliki skor Apgar menit kelima ≥7. Analisis statistik menunjukkan hubungan yang signifikan antara preeklampsia dan kelahiran prematur (p <0,007; OR = 2,54, 95% CI 1,34-4,83). Preeklamsia juga berhubungan dengan skor Apgar rendah pada menit ke 1 (p <0,042; OR = 2,03, % CI 1,07-3,85) dan menit ke 5 (p <0,046; OR = 2,42, 95% CI 1,08-5,41). Neonatus yang lahir dari ibu preeklampsia berhubungan dengan skor Apgar yang lebih rendah pada menit pertama (p <0,002; OR = 5,82, 95% CI 1,99-17,02) dan menit ke 5 (p <0,001; OR 17,31, 95% CI 2,15-139,54).*

Kesimpulan: *Ibu preeklampsia memiliki risiko melahirkan bayi prematur dan bayi dengan skor Apgar rendah.*

INTRODUCTION

Every year, 15 million infants were born prematurely. In fact, Indonesia is in the fifth rank among 10 countries with the largest number of preterm births, meaning that there are 675,700 or 15.5 preterm births per 100 live births in Indonesia.[1] Risk factors of preterm births are classified into maternal factors, fetal factors, and placental factors that influence births to occur spontaneously or non-spontaneously. One of the maternal factors is preeclampsia/eclampsia, reported as the most common systemic comorbidity by a number of 24.1% preterm births.[2]

Preeclampsia is an obstetric complication after 20 weeks of pregnancy with new onset of hypertension and maternal organ dysfunction.[3,4] Pathophysiology of the preeclampsia needs more investigation, although many theories have existed to explain the disease. Possible mechanisms include impaired trophoblastic differentiation, placental hypoxia, and endothelial injury due to maternal angiogenesis imbalance.[5,6] In low and middle-income countries, preeclampsia and its complications remain a major burden. The mortality and morbidity can happen for both mother and her infants.[7] Preeclampsia/eclampsia prevalence in some regions varies, ranging from less than 1 % in Angola to 8% in Brazil.[8] Surprisingly, higher number of preeclampsia has been reported in Indonesia. There were 13.5% of severe preeclampsia/eclampsia cases reported from Bangil and Kanjuruhan, at two district hospitals in East Java between April 2009-March 2010.[9] Reported in 2014, cases of preeclampsia at Dr. Soetomo Academic Hospital had increased from 27.88% to 32.48%.[10] Dr. Soetomo Academic Hospital located in Surabaya is the largest tertiary referral hospital for East Indonesian region. Therefore, patients referred to this hospital are who mostly have more complicated and severe diseases.

Previous studies concerning effects of preeclampsia still have debatable results. Some studies stated that preeclampsia is related to preterm birth, but some conclude otherwise.[11-14] Recent data regarding preterm birth cases among preeclamptic women have not been reported in Dr. Soetomo Academic Hospital. It is important to determine how these obstetrical and neonatal complications influence neonatal results. Common assessments to determine neonatal wellbeing immediately after birth are Apgar score. Apgar score is to asses color, heart rates, reflex irritability, muscle tone, and respiration by a given score of 0, 1, or 2 for each component.[15] Some studies shown that low five-minute Apgar score is related to increased relative risks of cerebral palsy[15] and neurological sequelae in early adulthood, such as neurological disability and low cognitive function.[16] A retrospective multicentre study in seven tertiary referral centres in Indonesia reported that asphyxia is the most frequent perinatal complication of preeclampsia (27%), defined by Apgar Score <6.17 Concerning the high prevalence of preterm births and preeclampsia plus alarming consequences, this study aims to analyse the relationships between preeclampsia, preterm birth, and implications on Apgar score.

METHODS

This study was an analytic study with a retrospective case-control design, conducted in Dr. Soetomo Academic Hospital, Surabaya, East Java. Ethical clearance was obtained from the Ethical Committee of Dr. Soetomo Academic Hospital, number 0572/KEPK/Ix/2018. Its data were collected from medical records of the Obstetrics and Gynaecology Department Delivery Room. Its samples were taken from total sampling of all births in a period of 1 January - 31 December 2017 and were divided into 2 groups. The first group, a case group, was women who had preterm delivery, and the second group, a control group, was women who had term delivery. Inclusion criteria in this study were singleton pregnancies and gestational age at birth <37 weeks. Stillbirth, fetal congenital abnormalities, oligohydramnios, preterm premature rupture of membranes, placenta previa, placenta accreta, fetal distress, pulmonary edema, thyroid abnormalities, Systemic Lupus Erythematosus, bacterial vaginosis infection, diabetes mellitus, heart abnormalities, kidney disorders, and malignancies were excluded as they may contribute to preterm birth.

Independent variable in this study was preeclampsia, defined by International Society for the Study of Hypertension in Pregnancy (ISSHP) as hypertension (blood pressure ≥149/90 mmHg) at 20 weeks gestation accompanied by one or more of the following conditions: proteinuria, dysfunction of other organs such as kidney failure, liver disorders, neurological and haematological complications, or fetal growth restriction.[3] Preeclampsia diagnosis was conducted by obstetricians. Dependent variable in this study was preterm birth, defined as livebirth at gestational age <37 weeks.[1] Clinical status of preeclampsia was divided based on the ACOG (American College of Obstetricians and Gynecologists) definitions.[4] Maternal characteristics and data of neonatal results were compiled for both groups and were presented as frequencies and percentages. Apgar score shown in infant's morbidity was measured at the first and fifth minute and was divided into groups of Apgar score <7 (low) and Apgar score ≥ 7 (normal).[18] All statistical analysis was conducted by using Chi-square test and Fisher's Exact test at 5% level of significance. P-values <0.05 were considered significant.

RESULTS

A total number of 945 deliveries were registered during this study, and 122 preterm deliveries were identified (12.91%). Among the 122 patients who had preterm delivery, 80 of them was included in the inclusion criteria and had complete medical records. Among the 823 total deliveries at term births, 80 of them were randomly sampled as a control group. Thus, 160 patients were included in the study.

There were only 70 preterm cases and 79 term cases with complete data for BMI variables. Mode of delivery in this study was divided into spontaneous vaginal delivery, assisted vaginal delivery (forceps, vacuum, manual aid) and caesarean section. In preterm preeclampsia group, there were 7 cases of spontaneous vaginal delivery, 5 cases of assisted vaginal delivery, and 32 cases of caesarean section. In preterm normotensive group, there were 30 cases of spontaneous vaginal delivery, 3 cases of assisted vaginal delivery, and 3 cases of caesarean section. Meanwhile, in term preeclampsia group, there were 4 cases of spontaneous vaginal delivery, 5 cases of assisted vaginal delivery, and 17 cases of caesarean section. In term normotensive group, there were 30 cases of spontaneous vaginal delivery, 3 cases of assisted vaginal delivery, and 21 cases caesarean section.

The most frequent mode of delivery in preterm group was spontaneous vaginal delivery, and in term group was caesarean section. However, when categorized into preeclampsia and normotensive groups, the most frequent mode of delivery in preeclampsia group was caesarean section (32 cases of caesarean section in preterm preeclampsia and 17 cases in term preeclampsia).

Distributions of maternal characteristics in both case and control groups can be seen in table 1 below.

Table 1 Maternal Characteristics

Maternal Characteristic	Preterm f (%)	Term f (%)
Age (year)		
<20	10 (12.50%)	3 (3.75%)
20-35	51 (63.75%)	62 (77.50%)
>35	19 (23.75%)	15 (18.75%)
Total	80 (100.0%)	80 (100.0%)
Body Mass Index (BMI)		
<18.5 (underweight)	1 (1.25%)	0 (0.00%)
18.5-24.9 (normal)	28 (35.00%)	27 (33.75%)
25-29.9 (overweight)	22 (27.50%)	28 (35.00%)
≥30 (obese)	19 (23.75%)	24 (30.00%)
Incomplete data	10 (12.50%)	1(1.25%)
Total	80 (100.0%)	80 (100.0%)
Parity Status		
Nulliparous	32 (40.00%)	27 (33.75%)
Primiparous	29 (36.25%)	26 (32.50%)
Multiparous	19 (23.75%)	27(33.75%)
Total	80 (100.00%)	80(100.00%)
History of Preterm Delivery		
Yes	6 (7.50%)	3 (3.75%)
No	74 (92.50%)	77 (96.25%)
Total	80 (100.00%)	80 (100.00%)
Mode of Delivery		
Spontaneous Vaginal Delivery	37 (46.25%)	34 (42.50%)
Assisted Vaginal Delivery	8 (10.00%)	8 (10.00%)
Caesarean Section	35 (43.75%)	38 (47.50%)
Total	80 (100.00%)	80 (100.00%)

Table 2 Clinical Status of Preeclampsia

Clinical Status	Preterm f (%)	Term f (%)
Chronic hypertension superimposed preeclampsia with severe features	15 (34.09%)	5 (19.23%)
Preeclampsia without severe features	2 (4.55%)	5 (19.23%)
Preeclampsia with severe features	22 (50.00%)	15 (57.69%)
HELLP syndrome (partial/total)	5 (11.36%)	0 (0.00%)
Eclampsia	0 (0.00%)	1 (3.85%)
Total	44 (100.00%)	26 (100.00%)

Among 160 births, 70 preeclamptic mothers and 90 normotensive mothers were found. Among 80 cases of preterm birth (case group), there were 44 cases of preeclampsia and 36 cases of normotensive patients. Then among the term group (80 cases), 26 cases of preeclampsia and 54 cases of normotensive were identified. As shown in the Table 2, clinical presentation of preeclampsia was assessed. In both groups, the most clinical status recorded was preeclampsia with severe features. However, cases of preeclampsia with severe features and chronic hypertension superimposed preeclampsia with severe features were found higher in the preterm group. HELLP syndrome cases were only found in the premature group, whereas preeclampsia progressing into eclampsia was only found in term group. The incidence of preeclampsia without severe features was more common in the term group (19.23% vs 4.55%).

Tabel 3 Neonatal Outcome Characteristics

Neonatal Outcome	Preeclampsia f (%)	Normotensive f (%)	p value	OR (CI 95%)
Gestational Age at Birth				
extreme preterm (<28 weeks)	2 (2.86%)	3 (3.33%)		
very preterm (28-<32 weeks)	9 (12.86%)	12 (13.33%)		
moderate preterm (32-<37 weeks)	33 (47.14%)	21 (23.33%)		
term (37-42 weeks)	26 (37.14%)	54 (60.00%)		
Total	70 (100.00%)	90 (100.00%)		
Birth Weight				
ELBW (<1000 grams)	5 (7.14%)	2 (2.22%)		
VLBW (<1500 grams)	8 (11.43%)	8 (8.89%)		
LBW (<2500 grams)	35 (50.00%)	32 (35.56%)		
NBW (≥ 2500 grams)	22 (31.43%)	48 (53.33%)		
Total	70 (100.00 %)	90 (100.00%)		
Apgar Score at 1st Minute				
<7	37 (52.86%)	32 (35.56%)	0.042	2.03 (1.07-3.85)
≥7	33 (47.14%)	58 (64.44%)		
Total	70 (100.00%)	90 (100.00%)		
Apgar Score at 5th Minute				
<7	19 (27.14%)	12 (13.33%)	0.046	2.42 (1.08-5.41)
≥7	51 (72.86%)	78 (86.67%)		
Total	70 (100.00%)	90 (100.00%)		

*ELBW: Extremely Low Birth Weight, VLBW: Very Low Birth Weight, LBW: Low Birth Weight, NBW: Normal Birth Weight

Table 3 divided the case and control group into preeclamptic and normotensive women to compare characteristics of neonatal outcomes. A majority of preeclamptic mothers (47.14%) gave birth at 32-<37 weeks of completed gestation. Most infants from preeclamptic mothers were born with birth weight of <2500 grams (50.00%). Low Apgar score at 1st Minute (<7) was found more in preeclampsia patients (52.86%) rather than in normotensive patients (64.44%). However at 5th minutes measurements, normal scores (≥7) were found in both preeclampsia

and normotensive group. Statistical analysis presented significant difference on Apgar score at 1st and 5th minutes between infants born from preeclampsia and normotensive women (p<0.005). The differences in Apgar score according to gestational age at birth is statistically significant in this study, as shown in table 4.

Tabel 4 Analysis of relationships between Apgar score and Gestational age at birth in preeclamptic mothers

Apgar Score	Gestational Age At Birth		p-value	OR (95% CI)
	<37 weeks	≥37 weeks		
First Minute				
<7	30 (68.18%)	7 (26.92%)		
≥7	14 (31.82%)	19 (73.08%)	0.002[a]	5.82 (1.99-17.02)
Total	44(100.00%)	26(100.00%)		
Fifth Minute				
<7	18 (40.9%)	1 (3.85%)		
≥7	26 (59.1%)	25 (96.15%)	0.001[b]	17.31 (2.15-139.54)
Total	44(100.00%)	26 (100.00%)		

a: Chi-Square Test; b: Fisher's Exact Test

Tabel 5 Analysis of relationships between preeclampsia and preterm birth

Preeclampsia	Preterm Birth		p-value	OR (95% CI)
	Yes	No		
Yes	44 (55.00%)	26 (32.50%)		
No	36 (45.00%)	54 (67.50%)	0.007	2.54 (1.34 – 4.83)
Total	80 (100.00%)	80 (100.0%)		

Table 5 pointed out that incidence of the preterm birth in preeclampsia was 44 (55.00%). According to the statistical analysis above, it could be concluded that there was a relationship between preeclampsia and premature birth. The mothers suffering preeclampsia could have the 2.54-fold risks of giving birth prematurely compared to normotensive women.

DISCUSSION

Compared to the national prevalence in 2010, rates of preterm birth in this study were lower (12.91% vs 15.5%). However, its number was higher compared to the global average of preterm birth rate in 2010 (11.1%).[19] The authors believe that changing patterns of obstetric care have contributed to this progress.

Similar characteristics of maternal age, BMI, parity status, and history of preterm birth were found in both groups. Most of patients in this study were in 20-35 years old group. Distributions based on the age of these patients are similar to a study in Cipto Mangunkusumo Hospital.[20] Nevertheless, both studies found that percentage of maternal age (<20 years old) in the preterm group was higher than in the term group. Fuchs's study confirmed an increased risk of preterm birth and spontaneous preterm birth that could occur for young women (20-24 years old). Low socioeconomic conditions and higher risks of medical complications mainly found in women who get pregnant at younger

age or women who delay their first pregnancy at later age.[21] Therefore, the risks of preterm birth could higher.

The highest proportion of maternal BMI occurred in a normal/ideal range (40.00%) in the case group. Meanwhile, most patients in the control group were overweight (35.44%) and normal (34.18%). However, the average BMI of the case and control groups was in normal ranges. The data of this study are similar to results of Tellapragada's study in India where 31 of 54 mothers with preterm labour (57%) had a normal BMI.[22] This might be because both studies were conducted in Asian developing countries (Indonesia and India) so that economic equality may be considered in terms of meeting nutritional needs.

A majority of the preterm group in this study was nulliparous (40.00%) and primiparous (36.25%). These findings are in line with trends of preterm deliveries in Taiwan[23] and in Jakarta.[20] A majority of the mothers in both groups did not have a history of preterm deliveries. Similar distributions were also found in a study at Arifin Achmad Hospital, Pekanbaru.[24]

Results of this study regarding the mode of delivery are in accordance to a multicentre study conducted by Aldika in Medan, Bandung, Semarang, Solo, Surabaya, Bali, and Manado. Severe preeclamptic/ eclamptic mothers in that study mostly had caesarean section (52.85%). Only 30.7% mothers had vaginal delivery and 16.5 % had vaginal delivery with vacuum or forceps extraction.[17] According to Adiasasmita's study (2015) in East Java, half of the women who had severe preeclampsia and eclampsia underwent caesarean section. The study also found that some cases (20-27%) progressed into near-miss status or death; therefore, a prompt management such as caesarean section was decided to save both mother and infant's lives.[9] Some of complications listed by Adiasasmita as near-miss inclusion criteria were pulmonary edema, cardiac arrest, cardiac rupture, cardiac failure, septic shock, liver dysfunction, respiratory dysfunction, coagulation and cerebral dysfunction, eclampsia, uterine rupture, ectopic pregnancy, intensive care admission, need resusitations, emergency hysterectomy, and referral to tertiary hospital.[9] Non reassuring fetal testing and maternal conditions such as the HELLP syndrome were also included as other indications of caesarean section.[6] On the other hand, most preterm and term normotensive mothers gave birth spontaneously probably due to more stable maternal and fetal condition at admission.

Percentage of clinical status of preeclampsia in this study is similar to a study at Khon Kaen University's Srinagarind Hospital, Thailand.[25] The study found that 50% severe features of preeclampsia were diagnosed among preeclamptic women, followed by 43.2% non-severe features of preeclampsia, and 6.5% HELLP syndrome. Most of the preterm birth cases were recorded in preeclampsia with severe features and HELLP syndrome cases (67.9%) and non-severe features of preeclamptic patients (23.4%).[25] Meanwhile, the authors in this study found that preterm delivery mostly occurred in preeclampsia with severe feature patients (50.00%) and chronic hypertension superimposed preeclampsia (34.09%). Preeclampsia without severe features was only 4.55% of preterm delivery. These finding similarities are probably because both studies were conducted in developing countries, tertiary referral hospitals; therefore, the diseases presented were often late or had already changed into severe cases. According to a report in 2011, 84% cases of preeclampsia with severe features in Dr. Soetomo Academic Hospital were referral patients.[26]

Dr. Soetomo Academic Hospital's protocol according to ACOG, recommends delivery at ≥ 37 weeks of gestation for preeclampsia without severe features and at ≥ 34 weeks of gestation for preeclampsia with severe features.[4,27] All of HELLP Syndrome cases in this study had delivered preterm birth probably due to the protocol that allowed termination of pregnancy after 48 hours of lung maturation conservative management at <34 weeks or termination after 34 weeks of completed gestation.[27] In this

study, the authors also found 1 mother who had preeclampsia with severe features that progressed into an eclamptic state at the time of delivery. Eclampsia is responsible for 0.2-0.5% potential risks of preeclampsia expectant monitoring at 34-47 weeks of pregnancy.[28]

This study found a significant relationship between the preeclampsia and the preterm birth (p=0.007). Preeclamptic women were 2.5-fold at risks of delivering preterm infants (Table 5). The findings are also in line with prior studies.[11,12] A study in Lampung by Nurmalasari reported 2.04-fold risk (CI 1.22-3.41) of preterm birth occurrence in preeclamptic mothers.[11] Roles of preeclampsia in 2 different types of preterm birth, spontaneous and iatrogenic, were assessed by a case-control study at Aberdeen Hospital, Scotland, England.[12] Mothers with preeclampsia were found to have 1.7 times higher risks of delivering premature infants due to spontaneous labour (95% CI 1.09–2.50) and 5.30 times (95% CI 4.48–6.28) risks of giving birth to iatrogenic premature infants.[12] On the other hand, Mutianingsih reported that there were no significant relationships between preeclampsia and preterm birth, mainly due to limited samples and study periods. Mutianingsih also stated that her study was conducted at West Nusa Tenggara General Hospital which has complete facilities and professional health providers, so the preeclampsia complications could be minimalized.[14]

There has been an assumption that preeclampsia can stimulate preterm labour with increased cortisol and cytokines production due to placental ischemia in preeclamptic mothers. Based on a literature study by Snegovskikh, excessive cortisol could trigger early activation of the fetal axis HPA resulting premature birth.[29] In preeclampsia, there is also a decreased activity of the placental enzyme 11β-HSD2 as proved by Aufdenblatten's study. The decreased activity of the enzyme makes the cortisol failed to be converted into cortisone (inactive form), resulting increased placental cortisol availability to the fetus. This excessive exposure may activate the HPA of the fetal axis, triggering premature labor.[30]

The results of this study also presented that infants born by preeclamptic mothers were born 50.00% of LBW, 11.43% of VLBW, and 7.14% of ELBW (Table 3). Different results were observed in infants born by normotensive mothers as 53.33% of them were born with normal birth weight more than 2500 grams. These results are in line with a finding of a study in Switzerland that stated 11β-HSD2 enzyme disorders in preeclampsia could have an impact on birth weight. In that study, reduced activities of 11β-HSD2 enzyme were also related to low birth weight. Reduced fetal growth could result from excessive placental cortisol exposure to the fetus.[30] A similar opinion was argued by Putra who stated that severe preeclampsia tended to develop in early pregnancies, so fetal growth could be compromised due to uteroplacental insufficiency.[31] Thus, the fetal tended to be born with low birth weight.

Another possible explanation regarding the relationships between the preeclampsia and the preterm births might be the low levels of PIBF (Progesterone Induced Blocking Factor) in preeclamptic patients. Faridz investigated placental PIBF expression by using preeclampsia models-pregnant mus musculus mice that were injected with anti-Qa2 on 1st and 4th day of pregnancy and were terminated on 16th day after remodelling of spiral arteries was completed. That research was based on a theory of Qa2 identical to HLA-G in humans. It showed a significant decrease of PIBF in preeclampsia compared to control models.[32] Literature studies mentioned that inadequate HLA-G expression could result lymphocyte cell activation and decreased sensitivity to progesterone. These results in decreased PIBF levels were expressed by trophoblasts, decidua, and lymphocyte cells in the placenta.[33] Decreased PIBF in preeclampsia could cause the preeclampsia to have a dominant Th1 cytokine condition and pro-inflammatory cytokines.[32,33] Moreover, the decrease in PIBF level could cause failed inhibition of phospholipase A2, resulting continuous prostaglandin synthesis.[34]

A prior retrospective cohort study in 2010

at Dr. Soetomo Hospital also found a significant relationship between the preeclampsia and the preterm birth (p = 0.003; 95% CI 1.301-3.497). Reportedly, mothers with preeclampsia were at risks of giving birth prematurely (86%), while risks in normotensive mothers were lower (74%).[35] Although this study used more specific exclusion and was conducted 8 years later, the authors found that preeclampsia has been still related to preterm birth. It showed that 55.00% of preterm infants were born by preeclamptic mothers. The number of preterm infants was lower compared to Kiswatin's study (62%) suggesting that clinical practice preeclampsia management had been developing ever since. Different methods used in both studies could also explain these results.

In this study, a majority of preeclamptic mothers had delivered preterm birth (62.86%), that 47.14% gave birth at 32-<37 weeks gestation, 12.86% at 28-<32 weeks and 2.86% at <28 weeks. Only 37.14% preeclampsia mothers were managed to deliver at term birth. Similar results reported by a study in Yorkshire, which found that 34.6% severe preeclamptic/eclamptic mothers gave birth at >=37 weeks gestation.[36] Conservative management in both studies is similar as it included close fluid management and magnesium sulfate for eclampsia prophylaxis. A majority of patients in both studies was also treated with oral rather than intravenous antihypertensive agents to promote gradual control of hypertension.[36] Unfortunately, the number of moderate preterm birth were still high in this study probably due to the hospital protocol for emergency delivery after 34 weeks gestation in severe preeclampsia cases. Hypertension in preeclampsia also can be plausible to cause preterm birth. Macdonald-wallis stated that shorter gestation was related to greater increase of systolic and diastolic blood pressure, particularly at 18-30 weeks and 30-36 weeks of gestation.[37]

The characteristics of neonatal outcomes in this study were also assessed based on the Apgar score recorded at the first and fifth minutes. 52.86% of infants born by preeclamptic mothers had Apgar score at 1st minute <7, while 64.44% of infants born by normotensive mothers had Apgar score at 1st minute ≥7. This study found Apgar score improvement at 5th minute, and a majority of neonates born by both groups had scores ≥7 (72.86% and 86.67%, respectively). These findings are consistent with results of Vats's study. In a case of hypertensive disorder of pregnancy, low Apgar score (<7) indicated fetal hypoxia at birth due to a decreased uteroplacental perfusion and an ischemia. Moreover, pregnancy complication like preeclampsia tended to require induction often followed by fetal distress.[38]

Based on this study, Apgar score at 1st and 5th minute, neonates of preeclamptic women were significantly lower than of normotensive women (p=0.042 and p=0.046, respectively). Preeclamptic women were 2.03 times at risks of having neonates with lower-first minute Apgar score and 2.42 times at risk of lower-fifth minute Apgar score. However, a previous study in Cipto Mangunkusumo Hospital reported that severity of preeclampsia increased more risks of having lower-first minute Apgar score (OR 2.00; 95% CI 1.38-2.91) rather than lower-fifth minute Apgar score (OR 1.26; 95% CI 1.06-1.51).[18] The Apgar score consisted of subjective components to evaluate infant's physiological condition at a one-time assessment immediately after birth.[15] Because both hospitals were teaching hospitals, the Apgar score was measured by neonatologists or neonatology residents. Inter-observer's interpretation variability in its diagnostic criteria could possibly lead to bias, as stated by Sungkar.[20]

Preeclamptic mothers were found at 5.82-fold risk of giving birth to preterm neonates (<37 weeks) with Apgar score at 1st minute <7 and 17.31-fold risk of giving birth to preterm neonates with Apgar score at 5th minute <7 in this study. The findings are in line with a study in Sweden secondary and tertiary hospital by Svenik.[13] Preterm birth could become the most evident risk factors for Apgar score at 5 minutes <7, particularly at gestational age 28 + 0–31 + 6 weeks (OR = 8 (5–12)) and gestational age <28 + 0 weeks (OR = 15 (CI 8–29)). Multiple gestation was reported as a significant factor for preterm

birth in that study (OR = 15 (CI 9–24)), but it was excluded in this study. Another significant risk factor for preterm birth in that study was preeclampsia. It significantly contributed to preterm birth before 32 weeks of gestation (OR = 5.5 (CI 3.4-8.9)), although its incidence was predicted and managed by considering the most severe preeclampsia accounts for medically indicated preterm birth.[13]

In the first minute, Apgar score of 4-7 could be considered as mild and moderate asphyxia, and score 0-3 could be considered as severe birth asphyxia.[39] Based on this study, the risk of lower Apgar score indicating birth asphyxia were magnified in preeclampsia and preterm condition. In cases of preeclampsia with severe features and impending eclampsia, a decision to deliver remote from term has become a major dilemma in clinical practice. Different approach and management in different hospitals may explain these different findings. Moreover, failed expectant management and decision to deliver preterm may be related to unfavorable perinatal outcome. This study found that expectant management in 9 of 22 (40.91%) cases of preeclamptic mothers who had delivered preterm were failed to lengthen gestation up to 33 weeks, and delivery ranged at 27-32 weeks due to spontaneous contractions and indicated extreme preterm birth in emergency cases. Nevertheless, unpredictable nature of preeclampsia requires standardized maternal intensive cares, labor control monitoring, best timing of delivery and NICU facilities to improve neonatal outcomes and survival.[38,40] Further studies are needed to investigate the differences between intensive care management, monitoring, and NICU facility on treating pregnancy complications in several central hospitals.

This study has some limitations. This research was a retrospective study using data from medical records. In addition, this study did not consider other socioeconomic risk factors such as maternal habits (smoking, alcohol consumption, drug consumption) and family income that might contribute to preterm birth. A prospective study with a category of spontaneous and iatrogenic preterm birth should be investigated in the future to specifically determine contributions of preeclampsia in different types of preterm birth.

CONCLUSION

It could be concluded that preeclampsia might be related to preterm birth and adverse perinatal outcomes, particularly on Apgar score. The preeclamptic mothers were at risks of delivering neonates with low Apgar score indicating asphyxia perinatal. The risk was even greater in cases of preterm preeclampsia. Intervention in modifiable risk factors of preeclampsia could prevent alarming consequences of preeclampsia complications both for maternal and neonatal well-being. Routine antenatal care and screening of preeclampsia within 12-28 weeks are strongly suggested to prevent late diagnosis, late arrival, late treatment, and progression into more severe cases.

CONFLICT OF INTEREST

There was no conflict of interest.

ACKNOWLEDGEMENT

The authors would like to express the best gratitude to Atika, S.Si, M.Kes from Department of Public Health, Universitas Airlangga, Surabaya, who help a statistical analysis in this study. The best gratitude is also for Dr. Reny I'tishom S.Pi., M.Si., contributing for manuscript preparation. The best gratitude is for officers of Medical Record Centre, Dr. Soetomo Academic Hospital, helping the data collection process.

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