Research Article

The Association between Preeclampsia and Newborn Hearing Loss

Hubungan antara Preeklamsia dengan Penurunan Pendengaran pada Bayi Baru Lahir

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Abstract

Objective : To analyze the relationship between preeclampsia (PE) and the newborn hearing loss.

Methods : This cross-sectional study was conductedat RSMH Palembang since December 2016 to July 2017, obtained 48 aterm neonates born from mother diagnosed with PE (11 PE and 37 severe PE). Measurements of neonatal hearing loss then performed using emission otoacoustic (OAE) in both ears by ENT division with categories interpretation of pass and referred. The mothers were physically checked and interviewed to obtain demographic data and obstetric history. After the data normality were proved by Shapiro Wilk test, we performed bivariate analysis using X2 test on demographic and obstetric characteristics of the mother, neonatal demographic characteristics, and determine the relationship of PE with OAE result.

Results : There were no significant differences in maternal and neonatal demographic characteristics in neonatal hearing loss (p> 0.05). No significant relationship was found between PE and OAE of both ear (right, p = 0.437; left, p = 0.368). There was difference of mean of SBP and DBP of mother in neonate OAE of both ears (p <0.05) with cut offpoint of SBP 160 mmHg and DBP 106 mmHg.There was a significant association between DBP (≥ 106 mmHg) of the mother and birth weight of the fetus (< 2.500 g) with referred OAE.

Conclusions : There was a significant association between neonatal hearing loss and maternal PE, determined primarily by maternal DBP, and neonatal birth weight.

Keywords : maternal blood pressure, OAE, preeclampsia.

Abstrak

Tujuan : *Untuk menilai hubungan preeklamsia (PE) ibu dengan penurunan pendengaran bayi baru lahir.*

Metode : *Penelitian observasi analitik dengan disain potong lintang dilakukan di RSMH Palembang sejak Desember 2016 sampai Juli 2017, diperoleh 48 neonatus aterm lahir dari ibu PE (11 PER dan 37 PEB). Neonatus dilakukan pengukuran pendengaran menggunakan otoakustik emisi (OAE) pada kedua telinga oleh divisi THT dengan kategori intepretasi refer dan pass. Ibu dilakukan pemeriksaan dan wawancara untuk memperoleh data demografi dan riwayat obstetri. Setelah normalitas data dibuktikan dengan tes Saphiro Wilk, dilakukan analisis bivariat menggunakan tes X2 pada karakteristik demografi dan obstetri Ibu, karakteristik demografi neonatus, dan menentukan hubungan PE dengan hasil OAE.*

Hasil : *Tidak ditemukan perbedaan signifikan karakteristik demografi Ibu maupun neonatus tehadap penurunan pendengaran neonatus (p>0,05). Tidak ditemukan hubungan signfikan antara kondisi PE dengan OAE kanan (p = 0,437) dan kiri (p = 0,368). Ditemukan perbedaan rerata TDS dan TDD ibu terhadap OAE kedua telinga neonatus (p<0,05) dengan cut off point TDS 160 mmHg dan TDD 106 mmHg. Ditemukan hubungan signifikan antara TDD (>106 mmHg) ibu dan berat lahir janin (>2500 gr) dengan OAE refer.*

Kesimpulan : *Terdapat hubungan bermakna antara penurunan pendengaran neonatus dengan kondisi preeklamsia ibu, yang ditentukan terutama oleh TDD ibu, serta berat lahir bayi.*

Kata kunci : *OAE, preeklamsia,tekanan darah usia reproduksi tidak hamil, vitamin D.*

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INTRODUCTION

Severe preeclampsia (PE) is a complication that affects 2-7% of pregnancies and causing vascular damaged that lead to maternal multiple organ failure and severe hypoxic conditions to the fetus in utero.[1]

A study conducted in 2008 revealed that 33% of infants from mothers with a history of severe PE experience hearing loss shortly postpartum. Other studies have also mentioned that the hearing loss also arises in the fetus of the mother with severe PE.[2]This indicates that hypoxia itself gives such a considerable influence on the hearing loss.[3]

Hearing loss of newborns from the mothers with severe PE showed a decrease in low frequency (125-500 Hz) which resembling a cochlear pathology condition. Decrease of blood flow will cause a decrease in the microcirculation of the cochlea, causing damage to the cochlear function. Decreased of blood flow to the internal hearing organ (nucleus cochlear hypoxia, cochlear nerve hypoxia, or direct cochlear damage organ) is the key of the pathogenicity of the sensorineural type hearing loss in the mother with severe PE.[4]Cochlear itself is very sensitive, especially in the apical part, to microcirculation decrease. Therefore, PE condition gives a high risk of sensorineural hearing loss.[5]

Examination with otoacoustic-emissions (OAE) has the advantage of not require expert expertise and very economical to be used as a postnatal screening tool. Having a high sensitivity and specificity (>90%) on peripheral hearing loss.[5] Thus, this study aims to analyze maternal PE relationship with the degree of newborn hearing loss with OAE.

METHODS

A cross-sectional study was conducted at the Obgyn Department and ENT Department of RSMH Palembang since December 2016 – July 2017. The study sample was all newborns from mothers with severe PE who were treated in the Obgyn Departement of RSMH Palembang and fulfil the inclusion and exclusion criteria. Samples were taken by consecutive sampling technique.

Samples were then classified into PE group and normal (control) group. Matching was performed at the aspect of age, number of gravidity, and parity. Newborns sample will undergo a hearing function test with OAE by the ENT colleagues. The results of the examination will be presented in tabular form and analyzed with SPSS ver 17.0.

The data are presented descriptively in the form of 2x2 tables and then bivariate analysis with X2 test and unpaired T-test to assess the relationship between risk factor and the observed output based on significance (p) 0.05 (95% CI). The tendency of risks factor to the outcome of neonatal hearing loss was assessed by odds ratio (OR).

RESULTS

Research has been conducted to assess the relationship between PE with newborn hearing loss examined with OAE. Forty eight-term neonates born, either vaginally or abdominally, form PE mother (11 PE and 37 severe PE). Normality test with the Shapiro Wilk test was obtained for all independent variable which resulted in a normal distribution (p> 0,05).

Sample Demographic Characteristics

The characteristics of maternal demography are shown in Table 1. The number of PE mothers was in the severe PE category (77.1%) and there was no significant difference in demographic characteristics between the severe PE and PE groups (p>0.05). Both groups have similar patterns of demographic characteristics, where the majority mother give birth at the ideal age (20-35 years), take medication during pregnancy, do not consume herbs during pregnancy, have no infection during pregnancy, and all have no deafness or hearing loss family history. In terms of birth method, it was known that the majority of PE groups underwent normal labour (54.5%) while the majority of the severe PE group underwent a cesarean section (56.7%).

Table 1. Characteristics of Maternal & Neonatal Demographics Subject (N = 48)

Demographic Characteristic	PE		Severe PE		*P- value*
	n	%	n	%	
Maternal Characteristic					
Maternal age (years)	31.3636 + 4,80151		31.19892 + 6.53128		0.935
<20	0	0	1	100	0.698
20-35	9	25.7	26	74.3	(0.718 – 0.672)
>35	2	16.7	10	83.3	
Gestational age	36.8182 + 1.07872		37.1622 + 1.16699		0.388
>37 weeks	7	18,9	30	81.1	0.246
<37 weeks	4	36.4	7	63.6	(0.146 – 0.346)
Drugs during pregnancy					
No	4	36.4	7	63.6	0.208
Yes	7	18.5	30	81.8	(0.228 – 0.198)
Herbs during pregnancy					
No	9	28.1	23	71.9	
Yes	2	12.5	14	87.5	0.200
Infection or fever during pregnancy					(0.221 – 0.196)
No	10	22.2	35	77.8	0.551
Yes	1	33.3	2	66.7	(0.561 – 0.540)
H/ deafness in family					
No	11	22.9	37	77.1	£
Yes	0	0	0	0	
Delivery mode					
Normal	6	28.6	15	71.4	0.389
Vaginal operative	1	50	1	50	(0.409 – 0.369)
Cesarean section	4	16.0	21	84	
Neonatal Characteristic					
Birth weight (<2500 gr)	31.3636 + 4,80151		2908.11 + 565.380		0.454 (-513.214 – 233.362)
No	7	18.4	31	81.6	0.153
Yes	4	40	6	60	(0.164 – 0.142)
Neonatal infection					
No	11	22.9	37	77.1	£
Yes	0	0	0	0	
Hyperbilirubinemia					
No	11	22.9	37	77.1	£
Yes	0	0	0	0	
Asphyxia					
No	11	25	33	75	0.339
Yes	0	0	4	100	(0.349 – 0.329)
Cephalic Trauma					
No	11	22.9	37	77.1	£
Yes	0	0	0	0	
Ear Malformation					
No	11	22.9	37	77.1	£
Yes	0	0	0	0	
APGAR Score					
Normal	2	28.57	5	71.43	0.513
Abnormal	9	2	32	78	(0.523-0.503)
NICU admission					
No	11	22.9	37	77.1	£
Yes	0	0	0	0	

** Chi Square test, 95%CI, £ Significancy cannot be evaluate*

Table 1 also showed no significant difference in neonates born from PE and severe PE groups. Nevertheless, there was asphyxia (n = 4) occurred in neonates born from severe PE mothers, but the absence of neonates treated in the NICU showed that asphyxia was mild and transient. The absence of this neonate characteristic difference indicates that severe PE and PE conditions do not significantly influence the neonatal outcomes.

Relationship of Neonates OAE with Preeclampsia

Table 2 indicates there is no significant relationship between the degree of PE with the occurrence of neonatal hearing loss on both ears. So it can be deduced that the degree of PE does not affect the incidence of hearing loss in newborns based on OAE examination. However, the analysis of X2which uses the category data has a huge bias, mainly due to small sample sizes. So the analysis continued on the relationship of SBP and DBP to the occurrence of OAE abnormalities, as well as multivariate analysis to determine the significant risk factors of OAE abnormalities based on maternal and neonatal variables.

Table 2. Neonates OAE Relationship with Preeclampsia and Blood Pressure (N = 48)

Risk Factor	OAE Dxt		*P-value*	OAE Sin		*P-value*
	Refer	Pass		Refer	Pass	
Severe PE	10 (83.3)	27 (75)	0.437*	11 (84.6)	26 (74,3)	0.368*
PE	2 (16.7)	9 (25)		2 (15.4)	9 (25,7)	
Sistole (mean+SD)	167.5+14.22	158. 61+10.185	0.022§	166.92+13.775	158.57+10.331	0.028§
Interval (min-max)	(150-200)	(140-190)		(150-200)	(140-190)	
Diastole (mean+SD)	111.67+ 11.146	101.11 + 7.848	0.001§	111.54+10.682	100.86+7.811	<0.001§
Interval (min-max)	(100-140)	(80-110)		(100-140)	(80-110)	
Total	12 (100)	36 (100)		13 (100)	35 (100)	

* Fisher exact test, 95% CI, § Independent T Test, 95% CI

Neonates Hearing Loss Risk Factors

Table 3 showed that only maternal risk factors for DBP (cut off point 106 mmHg) were significantly associated with neonatal OAE abnormalities, while other maternal risk factors were not significant (p> 0.250), so multivariate analysis was not performed. Similarly, the risk factors for neonatal shows only birth weight (<2500 grams) which significantly associated with neonates OAE abnormalities, while other risk factor were not significant (p> 0.250) and multivariate analysis was not performed.

Table 3. Bivariate Analysis of Maternal and Neonatal Risk Factors for Abnormal OAE (N = 48)

Risk Factor	OAE		*P-value*
	Refer	Pass	
Maternal Risk Factor			
Maternal age			
>35 years	6 (46.2)	10 (28.6)	0.310
<35 yeas	7 (53.8)	25 (71.4)	
Sistolic blood pressure			
>160 mmHg	11 (84.6)	26 (74.3)	0.702
<160 mmHg	2 (15.4)	9 (25.7)	
Diastolic blood pressure			
>106 mmHg	10 (76.9)	11 (31.4)	0.008
<106 mmHg	3 (23,1)	24 (68.6)	
Degree of PE			
Severe PE	11 (84.6)	26 (74.3)	0.702
PE	2 (15.4)	9 (25.7)	
Infection during pregnancy			
Infection (+)	1 (7.7)	2 (5.7)	0.999
Infection (-)	12 (92.3)	33 (94.3)	
Drug consumption			
Yes	10 (76.9)	27 (77.1)	0.999
No	3 (23.1)	8 (22.9)	
Herb consumption			
Yes	6 (46.2)	10 (28.6)	0.310
No	7 (53.8)	25 (71.4)	
History of Deafness in family			
History (+)	0 (0)	0 (0)	£
History (-)	13 (100)	13 (100)	
Mode of Delivery			
Cesarean Section	7 (53.8)	18 (51.4)	0.999
Vaginal delivery	6 (46.2)	17 (48.6)	

Neonatal Risk Factor			
Birth weight (g)			
> 2.500	7 (53.8)	31 (88.6)	0.016
< 2.500	6 (46.2)	4 (11.4)	
APGAR score			
10	3(23.1)	4 (11.4)	0.370
< 10	10 (76.9)	31 (88.6)	
Asphyxia			
Asphyxia (+)	1 (7.7)	3 (8.6)	0.999
Asphyxia (-)	12 (92.3)	32 (91,4)	

Fisher exact test, p = 0.05

DISCUSSION

In addition to the fetomaternal circulation, severe PE affects uteroplacental perfusion due to vasospasm. Systemic vascular insufficiency, especially the placenta, will interfere with the developmental process of fetus (hypoxic fetus). Hypoxia leads to hyperpolarization of inner hair cells that can resulting in changes in hearing neurons.[5]

Spontaneous release of the auditory neuron is the result of spontaneous release of the transmitter by hair cells. The stimulation of sound will cause depolarization of hair cells that will lead to increased release of chemical transmitters and neural jumps. In fetal hypoxia, hyperpolarization of hair cells will result in a decrease in the number of transmitters released and result in a decrease in nerve activity.[5]

Based on maternal demographic characteristics analysis no influence of maternal age, history of drug consumption, herbal medicine, infection during pregnancy and delivery method to neonatal hearing loss (p> 0.05). These findings are similar who examined maternal and placental factors for congenital hearing loss, suggesting that only funisitis (cord infection) was significantly associated with neonatal hearing loss (p = 0.05). While maternal age, parity, gestational age, delivery mode, use of antenatal drugs, and chorioamnionitis infection were statistically unrelated to neonatal hearing loss (p> 0.05).[6] The condition of funisitis was not investigated in this study, although funisitis appears to be a significant factor for congenital hearing loss.

Increase in interleukin-6 (IL-6) in umbilical cord blood, signalling a significant reduction in congenital hearing examined in neonates.[7] It was concluded that prenatal exposure to inflammation could damage the inner ear organ when a fetal inflammatory response occurs. On the other hand, the findings of chorioamnionitis did not significantly cause hearing impairment, so it is hypothesized that chorioamnionitis may not necessarily trigger a fetal inflammatory response, the outbreak of this response being confirmed only when there is an inflammatory cytokine on the umbilical cord.[6]

In some literatures, the age of preterm and low birthweight (LBW) are reportedly important facts or risks for congenital hearing loss.[7-9] A similar finding was found in this study, where birth weight <2.500 grams was significantly affected by congenital hearing loss diagnosed as *"refer"* to OAE examination. This finding is logical given that LBW conditions can be caused by premature gestational age so that the maturation of the inner ear organ has not been fully achieved, or in the case of term, the LBW condition indicates placental insufficiency and chronic fetal hypoxia occurring in preeclampsia resulting in deep hair cell hyperpolarization which may result changes in hearing neurons fetus.[5]

A contradictory finding was found in Apgar score variables, in which no significant association of Apgar scorewith congenital hearing loss was in contrast to previous studies. It has been hypothesized by previous studies that premature and LBW babies are associated with low Apgar score, so low Apgar score(which indicate fetal hypoxia) are also significantly associated with fetal hearing loss. However, this hypothesis is denied,where they found no significant relationship between Apgar scoreof 1 and 5 minutes with congenital hearing loss. It is hypothesized that Apgar score merely describe the condition of fetal well-being soon after birth and can not fully represent the intrauterine fetal hypoxia condition.[6,10] So that it can be understood when the LBW baby can have a hearing loss even though their Apgar score was good. Another

consideration of no significant association between Apgar values and hearing loss in this study was that Apgar values were assessed by different Pediatric residents so that the examiner bias could have an effect, and the Apgar 10 and <10 score categories resulted in inequality in assessments where the majority of neonates who were fit more often rated Apgar 9 instead of 10.

The next important variable in the study was drug use during pregnancy, where no significant association was found between the use of drugs during pregnancy with congenital hearing loss. The study did not specify what medications were used during pregnancy, so no analysis of the effects of each type of drug could be performed. In 2017, stated that prenatal antibiotic use has no effect on congenital hearing loss, and on the contrary, the use of corticosteroids has a positive effect which decreases congenital hearing loss in premature fetuses.[6]

The main maternal variable in this study was maternal blood pressure with a diagnosis of preeclampsia. In this study, it was found that blood pressure, especially diastolic with a *c*ut off of 106 mmHg, was significantly associated with congenital hearing loss, while systolic blood pressure with a *cut off of* 160 mmHg was not significantly related. These findings are similar to those who found a significant association between maternal blood pressure and congenital hearing loss, wherein the hearing impaired fetus was mainly from the maternal group with a mean systolic blood pressure of 156 ± 9.8 mm Hg (p <0.001) and diastolic blood pressure of 103.7 + 4.9 mmHg (p <0.001).[11]

Not many studies have described maternal blood pressure and compared women with normal preeclampsia with findings that differ from this study. For example, that there is no difference in neonatal hearing loss outcomes of the maternal group with hypertension in pregnancy and normal maternal groups;[12]Result and hypothesized that congenital hearing loss is caused by multifactorial factors, particularly environmental and genetic factors. Altuntas, however, found that women with HELLP syndrome were significantly associated with congenital sensorineural hearing loss.[2]These contradictory findings indicate that relationships between maternal blood pressure and congenital hearing loss need to be further investigated and use more detailed and comprehensive designs and tools.

Neonatal variables in this study found no significant association with congenital hearing loss, except birth weight. The same is also who states that perinatal characteristics of fetal age at delivery, birth weight, fetal sex, Apgar score, umbilical arterial pH, and postnatal neonatal decline (e.g. RDS, broncho-pulmonary dysplasia, intraventricular haemorrhage, periventricular leukomalacia, necrotizing enterocolitis, and seizures) are not associated with congenital hearing loss.[6]

This study was conducted on samples of PE mothers categorized as PE and severe PE; not much research has studied the effects of maternal preeclampsia on the outcome of hearing loss in neonates. Nevertheless, the authors acknowledge that this study has many shortcomings, among others: the number of samples is too small to be representative did not include normal mothers without PE as a comparison used cross sectionaldesign so it could not be known whether the hearing loss in some neonates is reversible or irreversible; used simple tool which was OAE that only gives the result of "refer" or "pass" without any translation of hertz level which is a problem in neonate hearing; didn't perform an analysis of the placenta using anatomical pathology examination to find out whether chorioamnionitis and funicitis were risk factors; didn't elaborate fully on research variables, for example drugs and herbs, types of prenatal infections, types of neonatal infections, Apgar score minutes 1, 5, and 10, and RDS types occured in neonates.

Further studies use prospective cohort design, larger sample size, healthy maternal as control, as well as advanced examination tools such as anatomic pathology, brainstem evoked response audiometry (BERA) ortransient evoked otoacoustic emission (TEOAE). Therefore, it is expected to provide more complete, informative, and valid relationships.

CONCLUSIONS

We noted that there was a significant association between neonatal hearing loss and maternal PE, determined primarily by maternal DBP, and neonatal birth weight.

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