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A MARKET AND A MAR	Original Research Paper	Neonatology		
	THE RELATIONSHIP BETWEEN THE NUMBER OF PLATELETS FOR NEWBORNS AND MATERNAL PREECLAMPSIA			
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Neonatal thrombocytopenia is the most common hematological disorder. Several studies have shown ABSTRACT that babies born to mothers of preeclampsia can cause neonatal thrombocytopenia. Early detection to identify changes in platelet newborns can be the basis of early management in reducing newborn morbidity and mortality. A diagnostics study with cross-sectional study of newborns according to the inclusion and exclusion criteria of preeclamptic and normal mothers was conducted at General Hospital Center Haji Adam Malik and University Sumatera Utara Hospital. Sampling uses total sampling between December 2018 until February 2019 among 84 infants with 15 babies were born to preeclamptic mothers and 64 babies were born to normal mothers. The cord blood sample is taken when the baby is born and then the platelet count is assessed. Data analysis used the chi square test (p < 0.05). There is a significant relationship between the number of platelets of newborns and preeclampsia (p = 0.005) with a prevalence ratio (PR) of 0.80

KEYWORDS : neonatal thrombocytopenia, preeclampsia

INTRODUCTION

Preeclampsia is a medical disorder found during pregnancy, labor and childbirth. Preeclampsia is a multisystem disorder characterized by a new onset of hypertension that occurs after 20 weeks of pregnancy with clinically relevant proteinuria.1,2 Preeclampsia affects 3% of pregnant women worldwide and is one of the most common medical complications in pregnancy.^{3,4}

Based on reports from the World Health Organization (WHO), preeclampsia occurs in 2 to 8% of pregnancies worldwide. Preeclampsia caused 16.1% of maternal deaths in developed countries, 25.7% in Latin America and the Caribbean 9.1% in Asia. Preeclampsia is a major cause of maternal mortality in developed countries.5 The incidence of preeclampsia in Indonesia is reported to reach 6%.6 Meanwhile, in PKU Muhammadiyah Yogyakarta, the incidence of preeclampsia was reported at 3.9% .7 Cases of preeclampsia in North Sumatra were reported in 3560 cases in 251 449 pregnancies (1.4%) in 2010. Maternal deaths from preeclampsia in dr. Pirngadi hospital was reported at 3.45% in 2007 to 2008, 2.1% in 2008-2009, and 4.65% in 2009 to 2010. $^{\circ}$

Neonatal thrombocytopenia is a hematological disorder that often occurs in neonates where it requires advice from the hematologist for treatment in preventing long-term death or disability.9 Thrombocytopenia that appears in the first 72 hours of life usually results from placental insufficiency and is caused by reduced platelet production. Fortunately most episodes are mild and are currently disappearing spontaneously.¹⁰

The prevalence of thrombocytopenia in neonates with preeclamptic mothers varies. Pritchard et al showed that the incidence of thrombocytopenia ranged from 9.2 to 36%.11 In another study, the incidence of thrombocytopenia associated with this disorder was estimated to be 1 per 100 live births and more likely to occur in premature infants and low birth weight infants.¹²

According to the study of Sunil et al 57.3% of infants born to mothers with gestational hypertension, preeclampsia and eclampsia syndrome had thrombocytopenia.13 Whereas Brazy JE et al noted that thrombocytopenia occurs in 36% of infants with preeclamptic and severe preeclampsia mothers.¹⁴

Early detection to identify early platelet changes in newborns of mothers with preeclampsia is very important as a basis for early management in reducing morbidity and mortality in newborns.^{11,12,15}

METHODS

Study Design

A diagnostic study with a cross-sectional design was carried out in December 2018 to February 2019 among 84 newborns in the central neonatology unit of the Haji Adam Malik General Hospital and North Sumatra University Hospital. The inclusion criteria are all newborns from preeclamptic mothers and from normal mothers. Exclusion criteria are infants born with multiple congenital and infants born to mothers with anemia and chronic hypertension.

All babies born to mothers who were in accordance with the inclusion and exclusion criteria were taken blood samples from the cord blood vessels as much as 1 mL and inserted into the EDTA tube provided. Then the EDTA tube that has been filled with blood is brought to the laboratory to be examined for the platelet count. Thrombocytopenia is said if the platelet count is $< 150,000/\mu$ L.

Data analysis used chi square test (p <0.005) to find the relationship between newborn thrombocytopenia and maternal preeclampsia. Data analysis was performed using Statistical Package for Social Sciences (SPSS) software. This study was approved by the Health Research Ethics Committee, Faculty of Medicine, University North Sumatra.

RESULTS

This study was conducted at H. Adam Malik Hospital and University Sumatera Utara Hospital Medan. A total of 84 newborns were included in this study. There were 15 preeclampsia patients and 69 normal patients. Most subjects (91.7%) were born at gestational age of more than 34 weeks. 56% of the subjects in this study were women. Most subjects (65.5%) were born to multigravida mothers. As many as 17.9% of mothers with preeclampsia and most subjects (3.6%)

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platelet levels <150000 mg/dL. The mean age of the mother is 30.3 years, while the average body weight, body length and head circumference are 2900 grams, 46.7 cm and 32.6 cm (Table 1).

The table 2 shows that of the four risk factor variables obtained only gestational age and low birth weight which have a significant relationship, with each p value of 0.017 and 0.0001. The relationship seen from gestational age and preeclampsia is the condition of the mother of preeclampsia will make the gestational age greater (\geq 34 weeks) with 8 times the risk while the condition of the mother with no preeclampsia will cause a smaller gestational age (<34 weeks). The relationship seen from birth weight and preeclampsia is the condition of mothers with preeclampsia will make birth weight smaller (<2500gr) with a risk of 13.3 times, while the condition of mothers with no preeclampsia will cause greater birth weight (> 2500gr).

Table 3 shows that babies born with thrombocytopenia will cause smaller birth weight (<2500gr) with a risk of 0.842 times, while babies born with no thrombocytopenia will cause greater birth weight (>2500gr).

The relationship between the number of platelets of newborns and preeclamptic mothers was assessed by the chi-square test. Based on the statistical analysis, it was found that there was a statistically significant association between platelet levels of newborns with maternal preeclampsia (Table 4).

Table 1 Demographic characteristics of subjects Table 2. Relationship between risk factors for birth and maternal preeclampsia

Variable	Preeclampsia		р	PR	CI 95%
	Yes (n / %)	No (n / %)			
Gender					
Boys	7 (18,9%)	30 (81,1%)	1,000	1,138	0,371 – 3,488
Girls	8 (17,0%)	39			
Gestational ag	le				
< 34 weeks	4 (57,1%)	3 (42,9%)	0,017	8,000	1,572- 40,723
\geq 34 weeks	11(14,3%)	66 (85,7%)			
Birth weight	•			•	
< 2500 gram	10(52,6%)	9 (47,4%)	0,0001	13,333	3.700- 48,047
≥ 2500 gram	5 (7,7%)	60 (92,3%)			
Parity					
Primigravida	5 (17,2%)	24 (82,8%)	1,000	0,938	0,287- 3,058
Multigravida	10(18,2%)	45 (81,8%)			

Table 3. Relationship between risk factors for birth and platelet newborns

Characteristics	n=84
Gender, n (%)	37 (44)
Воу	47 (56)
Girl	
Gestational age, n (%) ≤34 weeks >34 weeks	7 (8,3) 77 (91,7)

Parity, n (%)	29 (34,5)
Primigravida	55 (65,5)
Multigravida	
Preeclampsia, n (%)	15 (17,9)
Yes	69 (82,1)
No	
Neonatal Thrombocytopenia, n (%)	81 (96,4)
≥150000	3 (3,6)
<150000	
Mothers age, years, mean (SD	30,3 (5,6)
Body weight, gram, mean (SD)	2900,1 (682,5)
Body lenght, cm, mean (SD)	46,7 (3,7)
Head circumference, cm, mean(SD)	32,6 (1,8)

Table 4. Relationshi	o between	platelet	counts	of newbo	rns
and maternal preecl	ampsia				

Variable					
	Thrombocytope				
	nia				
	Yes	No	р	PR	CI 95%
	(n / %)	(n/			
		%)			
Gender					
Boys	3 (8,1%)	34	0,082	0,919	0,835-
		(91,9%)			1,011
Girls	0 (0,0%)	47			
		(100%)			
Gestation	nal Age				
< 34	1 (14,3%)		0,232	6,250	0,493-
weeks					79,280
≥ 34	2 (2,6%)	75			
weeks		(97,4%)			
Birth weig	ght				
< 2500	3 (15,8%)	16	0,010	0,842	0,693-
gram		(84,2%)			1,023
≥ 2500	0 (0,0%)	65			
gram		(100%)			
Parity					
	1 (3,4%)	28	1,000	0,946	0,082-
Primigra		(96,6%)			10,899
vida					
	2 (3,6%)	53			
Multigrav	4	(96,4%)			
ida	1	1	1	1	1



DISCUSSION

In this study it was found that the risk factors for female gender were more prevalent for the incidence of preeclampsia but this was not significantly related. This study differs from the study of Elsmen et al In 2006 which showed that male sex was associated with an increased risk of the incidence of preeclampsia.16 In theory it was found that male sex in the womb resulted in an increase in testosterone. So this is also suspected as one of the factors in the occurrence of preeclampsia. In pregnancy with the male sex it is found that there is a decrease in aromatase secretion which functions to metabolize testosterone to estrogen. This results in an increase in testosterone. In addition, there is a presumption of dysregulation of androgen signals along with the secretion of androgen receptors on the placenta which ultimately increases the frequency of complications associated with preeclampsia in the mother and fetus.17 In the study of Shiozaki et al it was found that female sex had a higher risk of preeclampsia and gestational hypertension.¹⁸

In this study it was also found that the incidence of preeclampsia most often occurred at slow onset (\geq 34 weeks) and this was significantly associated with the incidence of preeclampsia with a risk of 8 times. In the 2015 Harmon et al study found preeclampsia recorded 3.8% of all pregnancies in Norway. The risk of the fetus with preeclampsia decreases with increasing gestational age, but at 34 weeks remains 7 times higher than pregnancies without preeclampsia.19 The results of the study of Elsmenn et al also said there was a link between late-onset preeclampsia and male sex whereas early onset preeclampsia was associated with premature and the possibility that the fetus was female.¹⁶

In our study it was found that the condition of mothers with preeclampsia would make birth weight smaller (<2500gr) with a risk of 13.3 times. In this study, it was also found that the most prevalent in low birth weight (LBW) as much as 53.8% and at very low birth weight (LBW) were found as much as 50%. The results of a 2004 study by Lau et al also showed that significant preeclampsia caused low birth weight. Low birth weight in babies born to mothers with preeclampsia can occur because babies are born less months or enough months but experience growth disorders.20 Impaired fetal growth can occur due to retroplasenta circulation disorders where arteriole spasms cause fetal asphyxia and long-lasting spasm can disrupt fetal growth. Spasms of arterioles that lead to important organs in the body that lead to important organs in the body can cause a decrease in blood flow to the retroplasenta resulting in disruption of exchange of CO2, O2 and nutrients to the fetus.²

Preeclampsia causes reduced uteroplacental perfusion which causes the unique pathogenic process, reduced blood flow can cause baby's birth weight to be disrupted and if severe can cause fetal death and if the spasm lasts long can interfere with fetal growth pregnancy. This is due to the occurrence of vasospasm and hypovolemia with the result that the fetus becomes hypoxic and malnourished, so that babies are often born prematurely.²⁰²¹

In this study it was also found that most preeclampsia mothers were found in the multigravida group compared to primigravida mothers but there was no significant relationship. As with age, the risk factors for this parity still have debate. The relationship between parity with preeclampsia, namely women who are primigravida have a greater risk than multigravida women. This is supported by the results of a study that states that nulliparous women have a risk of 2.91 times compared to multiparous ones. In other studies there was no association between these factors and preeclampsia.²²

This study also found an association between risk factors where male sex was more prevalent for thrombocytopenia but this was not significantly related. This study is similar to the 2013 Ulusoy et al study which stated that the prevalence of thrombocytopenia was higher in male sex, this was due to the state of neonatal septicemia.23 In a study Kent et al reported that the risk of intracranial bleeding and septicemia was higher in male neonates .24 Bhat et al study also shows that thrombocytopenia is more common in male sex.²⁵

In this study it was also found that the incidence of thrombocytopenia will cause the baby to be born at gestational age ≥ 34 weeks and this is not significantly related. This study is different from the study conducted by Ulusoy et al. Which concluded that as many as 88% of infants suffering from thrombocytopenia were premature and 46% of them were caused by infection requiring transfusion.²³

In this study also found that babies born with thrombocytopenia will cause smaller birth weight (<2500gr) with a risk of 0.842 times. In this study, it was also found that the most found in low birth weight (LBW) of 7.7% and at very low birth weight (VLBW) were found as much as 33.3%. According to the research of Wiedmar et al It was also mentioned that thrombocytopenia most often occurs in low-birth infants. The most frequent causes of this disorder are mothers with preeclampsia, diabetes mellitus, neonatal sepsis and stunted fetal growth.26 Parity also affects the incidence of thrombocytopenia where in our study the most thrombocytopenia was found in the multigravida group compared to mothers but not significantly associated.

This study also concluded that there was a significant relationship between the number of platelets of newborns and the condition of maternal preeclampsia where p values of 0.005 were obtained. The pathogenesis of thrombocytopenia among infants born to mothers with preeclampsia is not known.27 The main mechanism produced by Roberts and Murray's research is that preeclampsia and fetal hypoxia produced have a direct depressant effect on megakaryositopoiesis and fetal platelet production.¹⁰

To conclude, In this study there was a relationship between platelet levels of newborns and the condition of preeclampsia in the mother. In addition, there are risk factors that cause preeclampsia and thrombocytopenia.

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