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ORIGINAL RESEARCH

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THE EFFECT OF ANEMIA ON THE INCIDENCE OF PREMATURE RUPTURE OF MEMBRANE (PROM) IN KERTHA USADA HOSPITAL, SINGARAJA, BALI

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Abstract

Background: Premature Rupture of Membranes (PROM) causes morbidity and mortality complications in both maternal and perinatal. Pregnancy with anemia where low hemoglobin level which is less than 11.1 g / dL can be the cause of PROM through biological mechanisms and mechanisms of disease.

Objective: This study aims to compare the risk of PROM between anemic maternal mothers and non-anemic maternal mothers.

Methods: A case-control study was conducted on the maternal mothers at Kertha Usada Singaraja Bali Hospital, with 106 cases and 106 controls, using maternity medical records data in January-December 2016. The cases and controls were adjusted to the parity. The data were collected using questionnaires consisting of 2 parts: the first part was about the demographic characteristics, and the second part was about the time of membrane rupture and hemoglobin level at the delivery. The obtained data were analysed using descriptive and analytic statistics on the computer program.

Result: On univariable analysis, the prevalence of PROM equalled to 28,3% in maternal anemia group. In bivariate analysis, the risk factors of were anemia status, maternal activity, and maternal age ($p < 0.05$). A multivariable analysis of conditional logistic regression analysis, controlling the possibility of confounding factors, showed that pregnant women with anemia would be at risk of PROM 3.59 times greater than non-anemic mothers (OR = 3.59, 95% CI = 1.82-7, 09).

Conclusion: The risk of PROM is higher in anemic maternal mothers than in non-anemic mothers, after homogenising with parity variables.

Keywords: premature rupture of membranes; anemia; Hb level

INTRODUCTION

Premature rupture of membranes is an obstetric condition in which an amniotic leak occurs at least one hour before the onset of labour, complicating 5-10% of all deliveries ([Caughey, Robinson, & Norwitz, 2008](#)). For pregnant women, premature rupture of membranes may increase the incidence of maternal morbidity and mortality, including *chorioamnionitis*, *endomyometritis*, postpartum hemorrhage, pelvic abscess, and an

increased chance of cesarean delivery ([Rouse et al., 2004](#)). Low hemoglobin levels which were less than 11.1 gr/dl during pregnancy is suspected as the primary cause of the infection that can result in premature rupture of membranes ([Ferguson, Smith, Saleniaks, Windrim, & Walker, 2002](#)). Anemia may affect the strength of body response to infections and immune function that can lead to the decrease of natural cell capability

([Oppenheimer, 2001](#)). In Singaraja, there is a tendency of increasing premature rupture of membranes cases and anemia during partum process for the last three years ([Dinkes, 2016](#)). The cause of premature rupture of membranes is most likely multi-factorial. The effects of anemia are not only on the mother but also on the fetus in pregnancy as well as pregnancy outcomes such as early rupture of membranes, the researcher compared postpartum women with premature rupture of membranes and those who did not suffer from premature rupture of membranes to see the occurrences of anemia.

METHODS

Study design

The study applied a retrospective cohort study with a hospital-based control case design (1:1).

Settings

The study was conducted from 25 September to 25 October 2017 at Kertha Usada Singaraja Bali Hospital. Kertha Usada Hospital Singaraja Bali is a referral hospital in Buleleng district. Kertha Usada Hospital equipped with medical facilities and equipment with a total capacity of 300 beds. Human resources Kertha Usada Hospital consist of 313 people, 29 specialist doctors, 15 general practitioners, two pharmacists, 174 nursing paramedics and 106 non-medical personnel. Kertha Usada Hospital facilities, include Emergency Unit, Laboratory, Pharmacy, Nutrition Installation, Hemodialysis, Operating Room, Intensive Care Unit (ICU), Neonatal Intensive Care Unit (NICU), Intermediate Care Room, delivery room, radiology (X-ray and CT-Scan), and three units of the ambulance. Referrals received at Kertha Usada Hospital includes maternal and child health such as delivery. Birth referrals received by the Kertha Usada hospital in 2016 were majority due to premature rupture of membranes. Premature rupture of membranes cases in 2016 at Kertha Usada hospital reached 256 out of total 803 births. Normal deliveries were 366 incidences, and delivery with cesarean section was 419. The causes of childbirth with cesarean section

were due to fetus position abnormalities, prolonged labour and premature rupture of membranes.

Research subjects

The study was conducted using medical records data of maternity from January to December 2016 to identify anemia effects on premature rupture of membranes occurrences. A total of 106 maternity mothers of premature rupture of membranes used as case group and 106 maternity mothers without premature rupture of membranes as control group included in this research. In case of a group, premature rupture of membranes is diagnosed by medical professionals like midwives or doctors at Kertha Usada Hospital Singaraja Bali. The control group consisted of the maternal mother without premature rupture of membranes. Case and control groups were matched (1: 1) based on parity. Those 212 maternal mothers were between nullipara and gran multiparaparity during the study conducted. Both cases and control groups used the same questionnaire for data collection. The inclusion criteria in this study were pregnant women who gave birth with gestational age (37-42 weeks), and single fetus alive. The gestational age was determined by the first day of the first menstrual period. The exclusion criteria in this study were pregnant women with multiple pregnancies, infants with a congenital anomaly, intrauterine fetus death, maternity mothers who had the chronic illness (diabetes mellitus, hypertension, asthma, heart attack).

Instrument

Data collection was conducted by self-administered questionnaires using secondary data from Maternity Medical Record at Kertha Usada Hospital Singaraja Bali from January to December 2016. The data were collected using a questionnaire comprising two parts: the first part was about demographic characteristics, and second part consisted of anemia and hemoglobin levels during labor.

Ethical consideration

The research was conducted after obtaining the approval or letter of research ethics from

'Aisyiyah University of Yogyakarta's Ethics Committee on August 16, 2017, with the number 01 / KEP-UNISA / Exe / VIII / 2017. The research was reviewed and approved by the director of Kertha Usada Hospital Singaraja Bali with number 507 / RSU-KU / IX / 2017 on September 19, 2017. Confidentiality well maintained during research by using anonymous techniques (respondents are identified by code number to ensure confidentiality).

Data analysis

The data were analysed using a computer program. For better understanding, the information was tabulated using univariable, bivariable and multivariable analysis. The result of the univariable analysis presented in frequency and percentage. The bivariable analysis was done to test the relationship between dependent variable and independent variables, such as premature rupture of membranes and anemia. The statistical test used Mantel-Haenszel (χ^2 MH) test, with significance level $p < 0.05$ and confidence interval (95%). The strength of the relationship was seen from the odds ratio (OR) between anemia and premature rupture of membranes incidence. The multivariable analysis used

conditional logistic regression with a significance level of $p < 0.05$ and confidence interval (95%). Modeling in conditional logistic regression shows 95% confidence interval (CI) value, AIC (Akaike's Information Criterion) to see how far all variables in each model predict the risk of premature rupture of membranes (PROM).

RESULTS

Distribution frequency of research subject's characteristic

Based on the data in **Table 1**, the status of anemia, the most dominant factor of maternal mothers who did not experience premature rupture of membranes did not suffer from anemia which had Hb ≥ 11 gr/dL of 33.1%. Based on the characteristics of the mother's occupation, the most commonly found in mothers who did not experience premature rupture of membranes were mostly unemployed (34.4%). According to the characteristics of maternal age, the most dominant was mothers who suffered premature rupture of membranes was the risky age that was in the age range of < 20 and > 35 years (29.7%).

Table 1 Distribution frequency of research subject's characteristic

Variables	PROM		Without PROM		Total	
	n=106	(%)	n=106	(%)	n=212	%
Anemia Status						
Anemia	60	28.3	36	16.9	96	45.3
Without Anemia	46	21.7	70	33.1	116	54.7
Mother's occupation						
Working	61	28.8	33	15.6	94	44.3
Unemployed	45	21.2	73	34.4	118	55.7
Mother's age (years)						
< 20 and > 35	63	29.7	44	20.8	107	50.5
20-35	43	20.3	62	29.2	105	49.5

The effect of anemia on the rate of premature rupture of membranes

The bivariable analysis was conducted to examine the relationship between dependent variable and independent variable, i.e. Premature rupture of membranes and anemia variables. The statistical test used Mantel-Haenszel (χ^2 MH) test, with significance level

$p < 0.05$ and confidence interval (95%). The strength of the relationship was seen from the odds ratio (OR) between anemia and the incidence of premature rupture of membranes. Analysis of the effect of anemia on the rate of premature rupture of membranes presented in Table 2.

Table 2 Analysis of *Mantel-Haenszel* parity equivalent to anemia and PROM

Variable PROM	Without PROM				χ^2_{MH}	p	OR _{MH} (CI 95%)
	Anemia status						
	Anemia		Without anemia				
n	(%)	n	(%)				
Anemia status							
Anemia	30	28.3	30	28.3	10.97	0.0009	3.59
Without anemia	6	5.7	40	37.7			(1.82-7.09)

Information : χ^2_{MH} = *Mantel-Haenszel* test p<0.05. OR_{MH} = (OR) *Mantel-Haenszel* (CI 95%)

Based on the result of the analysis on **Table 2**, it showed that anemia on maternal mothers had a significant correlation with PROM occurrences by looking at p-value= 0.0009 and OR = 3.59 (95% CI: 1.82-7.09). It can be

interpreted that maternal mothers with anemia would have three times higher risk of experiencing PROM compared to those who did not have anemia.

Table 3 Analysis of *Mantel-Haenszel* parity equivalent to occupation and age with PROM

Variable PROM	Without PROM				χ^2_{MH}	p	OR _{MH} (CI 95%)
	Occupation						
	Working		Unemployment				
n	(%)	n	(%)				
Occupation							
Working	19	17.9	42	39.6	14.98	0.0001	2.93
Unemployment	14	13.2	31	29.3			(1.66-5.17)
Mother's age (years)							
<20 and >35	30	28.3	33	31.2	6.81	0.0091	2.09
20-35	14	13.2	29	27.3			(1.20-3.63)

Information : χ^2_{MH} = *Mantel-Haenszel* test p<0.05. OR_{MH} = (OR) *Mantel-Haenszel* (CI 95%)

Table 4 Analysis of conditional logistic regression on anemia impact to PROM occurrences

Variable	PROM			
	Model 1	Model 2	Model 3	Model 4
	OR (CI 95%)	OR (CI 95%)	OR (CI 95%)	OR (CI 95%)
Anemia Status				
Anemia	3.59*** (1.82-7.09)	2.56* (1.24-5.24)	3.55*** (1.78-7.08)	2.53* (1.22-5.24)
Without Anemia	1	1	1	1
Occupation				
Working		2.59** (1.37-4.92)		2.59** (1.35-4.96)
Not working		1		1
Mother's age (years)				
<20 and >35			2.14* (1.18-3.85)	2.12* (1.16-3.87)
20-35			1	1
N	212	212	212	212
AIC	259.5	252.7	255.0	248.5

Information: OR= odds ratio with CI= Confidential Interval (95%), AIC= Akaike's Information Criterion, 1 = reference. Sig *p<0.05, **p<0.01, *** p<0.001

From the analysis result of **Table 3**, it shows that the occupation of the mother had a significant relationship with the incidence of PROM, by looking at the value p = 0.0001 and

OR = 2.93 (95% CI: 1.66-5.17). It can be interpreted that pregnant women who work will have a twice higher risk of experiencing PROM than those who do not work. Maternal

age has a significant relationship with PROM incidents, by looking at the values $p = 0.0091$ and $OR = 2.09$ (95% CI: 1.20-3.63). It can be interpreted that mothers who have a risky age that is in the age range <20 and ≥ 35 years at the time of pregnancy will have a twice higher risk to experience PROM than those who are 20-35 years.

Multivariable Analysis

Seeing whether occupation and age were confounding factors that changed the anemia effect on PROM incidence, conditional logistic regression analysis was performed with a significance level of $p < 0.05$ and confidence interval (95%). Modeling in conditional logistic regression shows odds ratio (OR) value, confidential interval (CI) 95%, and AIC (Akaike's Information Criterion) to see how far all variables in each model predict the risk of premature rupture of membranes.

The result of analysis model in **Table 4** used conditional logistic regression. Model 3 was chosen as a parsimonious model that is the best model to predict the risk of premature rupture of membranes. Thus, model 3 does not change the value of OR and significance value. Prevent the occurrence of PROM then the age of the mother should be considered.

DISCUSSION

The results of this study presented that maternal anemia in women had a significant association with PROM occurrences. Pregnancy with anemia will have three times higher risk than those without anemia. Low hemoglobin levels (<11.1 g / dL) are associated with premature rupture of membranes, presumably low levels of hemoglobin are the initial symptoms which do not appear so that can cause infection ([Ferguson et al., 2002](#)). Other studies say anemia that occurs early in pregnancy in which low blood hemoglobin levels is <11 g /dL may increase the risk of PROM compared to normal hemoglobin levels in preterm pregnancy ([Zhang, Ananth, Li, & Smulian, 2009](#)). Anemia of iron deficiency may increase

risk factors for maternal infection ([Allen, 2001](#)). Meanwhile, research conducted mentions that 59.6% of anemic mothers experience premature rupture of membranes, which in this study showed a significant relationship between anemia status and premature rupture of membranes, pregnant women with anemia had a 2.4 times greater risk compared with non-anemic pregnant women ([Pusparini, 2013](#)).

An imbalance rate between the need and intake of iron during pregnancy will lead to deficiency resulting in anemia. In biological mechanisms, anemia is found to affect the pregnancy outcomes ([Allen, 2001](#)). The decrease in hemoglobin or anemia causes a decreased amount of oxygen transported to the tissues, potentially increasing the risk of premature rupture of membranes due to hypoxia in the tissues. Anemia can lead to hypoxia in the tissues, and anemia of iron deficiency may increase serum concentrations of *norepinephrine*, causing maternal and fetal stress. The incidence of anxiety in pregnancy will stimulate the synthesis of hormone Corticotrophin Releasing Hormone (CRH). The presence of elevated CRH concentrations can lead to premature birth, hypertension in pregnancy, preeclampsia and PROM. The relationship between anemia and infection may be caused by increasing ability of phagocytes activity and rising bactericidal, resulting in a decrease in immune cells resulting in a proliferation of T and B cells that can cause infection ([Lone, Qureshi, & Emmanuel, 2004](#)).

The results of this study state that the occupation of the mother has a significant relationship with the incidence of PROM. Pregnant women who work will have a twice higher risk of experiencing PROM than those who do not work. Mothers who work outside the home could increase the incidence of PROM, the more factors that can cause fatigue, the higher the risk of another experiencing PROM ([Newman et al., 2001](#)). The results of other studies say that the pattern of pregnant women's work affects the energy needs; physical work performed too heavy and

exceeded eight hours per day during pregnancy may cause fatigue. Fatigue in work causes weak *corion* amnion, which can cause premature rupture of membranes ([Tahir, Seweng, & Abdullah, 2012](#)).

The results of this study indicate that maternal age has a significant relationship with the incidence of PROM. Mothers aged <20 and ≥35 years of age during pregnancy will have a twice higher risk for PROM than mothers aged 20-35 years ([Tahir et al., 2012](#)). Iron deficiency anemia is likely to cause reproductive disorders such as the risk of maternal infection. Lack of iron effect immune function. Anemia can alter the proliferation of T cells and B cells and reduce the cell's ability in do phagocytes activity, decrease cell activity and bactericidal. The presence of infection is a risk of preterm birth. The presence of bacteria or inflammation of cytokines in amniotic fluid or the *chorioamniotic* membrane has a strong association with PROM and premature birth incidences ([Allen, 2001](#)).

The Kovavisarach study says that there is no difference in the risk of PROM in the risky age group and the age group which is not at risk ([Kovavisarach & Sermsak, 2000](#)). A pregnancy that occurs at <20 years old or too young often causes complications for the mother and fetus; this is due to immature reproduction organs. The small reproductive organ at <20 years of age produces the uterus to be unable to support the pregnancy adequate; the amniotic membranes are naive and susceptible to tears that may cause premature rupture of membranes ([Prawirohardjo, 2008](#)).

As the age grows, it will decrease the ability of the reproductive organs to perform its functions. The decrease in service of the reproductive organs also affects the process of embryogenesis, the quality of the ovum also decreases, which is why pregnancy in old age is at risk for abnormal fetal development, congenital abnormalities as well as other conditions that interfere with pregnancy and childbirth such as labour with premature

rupture of membrane. As a result, it makes easier to break prematurely ([Cunningham, Leveno, Bloom, Spong, & Dashe, 2014](#)).

CONCLUSION

The risk of premature rupture of membranes was higher in the maternal anemia than the mothers without anemia, after homogenised with the parity variable. The maternal age had a significant relationship with the incidence of early rupture of membranes. Mother's age was not a confounding factor of premature rupture of membranes occurrences; it means that in the context of intervention to prevent the event of premature rupture of membranes, mother's age should be considered.

Declaration of Conflicting Interest

None declared.

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Author Contribution

All authors contributed equally in this study.

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