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Factor related to preterm premature rupture of membrane among pregnant women

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ABSTRACT

The incidence rate of premature rupture of membranes in Yogyakarta, Indonesia was 10.1%, the highest rate in Indonesia. This study's goal was to determine factors related to premature rupture of membranes among pregnant women in Sardjito Hospital. There were 220 pregnant women, 110 in the premature rupture of membranes or case group and 110 no premature rupture of membranes as control group. Urinary tract infection, anemia, and preterm premature rupture of membrane and the characteristics were the research factors. The Chi-square test and logistic regression were used to examine the data. Secondary data from medical records for the period January 2021 December 2022 was taken. Result of this study showed that 49.1% of the pregnant women in the case group had anemia, and 47.3% had urinary tract infections. In the control group had anemia 30.9% of pregnant women, while urinary tract infections infected 61.8% of them. Urinary tract infections and anemia were associated with a greater incidence of preterm premature rupture of membranes, according to a bivariate analysis with p-values of 0.042 and 0.009 (p-value=0.05). Anemia was the most significant factor associated with the incidence of preterm premature rupture of membranes (OR=2.26).

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1. INTRODUCTION

In Indonesia, the maternal mortality rate is still relatively high. There were 4,221 fatalities in 2019. 4,627 more maternal deaths are predicted to occur in Indonesia in 2020 [1]. According to the 2018 National Risk Assessment Report from the Republic of Indonesia's Ministry of Health, Yogyakarta was the province with the highest rate of premature rupture of membranes (PROM) was 10.1%. Previois data showed that 4.91% of pregnancies had amniotic fluid discharge issues [2]. Many measures have been taken to address it, but it remains unresolved [3], [4]. According to the findings of the perinatal maternal audit, preeclampsia, infection, diabetes mellitus, heart disease, brain tumors, and hemorrhage were the most common diagnoses for reasons of maternal death in Sleman Regency [5]. The premature rupture of the membranes is one of the reasons for infection [6], [7]. Preterm premature rupture of membranes not only puts the mother at risk but also puts the fetus at risk, which can have long-term effects such as cerebral palsy, neurodevelopmental problems, retinopathy, and bronchopulmonary dysplasia in neonates [8]. The cause of premature birth half more pregnant women are preterm premature rupture of membranes [9].

At RSUP Dr. Sardjito Yogyakarta, there are quite a few instances of pregnant women who experience PPROM. Out of a total of 651 pregnant and postpartum patients at Dr. Sardjito General Hospital,

76 cases contain 60 PPROM cases and 16 PROM cases or around 9.22% and 2.46%, respectively occurred. Some of these instances included an infection. PPROM are less common and less severe when maternal risk factors are promptly identified [10], [11].

Many factors influence the incidence of premature rupture, including socio-economic status, smoking history, sexually transmitted diseases, urinary tract infections, pregnancy history, miscarriage history, history of early childbirth, bleeding history, mother's age, polihidramnion, twin pregnancies, drug abuse history, and maternal nutritional status [12]. Urinary tract infections are one of the risk factors for PPROM [13]. PPROM happens when the fetal membranes are stretched and a microbial infection causes the release of cytokines and other inflammatory substances that weaken the membranes and produce collagenolysis, which is mediated by mechanical disruption [14]. Anemia in pregnant women is another factor that affects the development of PPROM. Anemia can influence the growth of T and B cells, decrease phagocytic activity, decrease cell activity, and reduce bactericidal activity, leaving the body vulnerable to infection [15]. PPROM incidence control efforts are still urgently required. This study goals were determined factor related to premature rupture of membranes among pregnant women in RSUP Dr. Sardjito Yogyakarta from January 2021 to December 2022.

2. METHOD

This study used a case control study used secondary daya of pregnant women in the Delivery Room of RSUP Dr. Sardjito Yogyakarta from January 2021 to December 2022. The population of this study was all pregnant women aged of pregnancy less than 37 weeks who were hospitalized in the Delivery Room, for a total of 846 pregnant women. Pregnant women were divided into the case group, with PPROM, and the control group, without or not PPROM. The cases of preterm premature rupture of membranes, out of a total of 145 cases, 20 did not including for the inclusion criteria, and 125 involved the inclusion criteria. The method of determining the case group sampling is by sorting from the top to number 110. In the control group, the sampling method is by probability proportional to size sampling. From a total sample taken of 701 pregnant women, divided by the number of months, namely 24, five samples were taken from each month, namely five, and by looking at the inclusion and exclusion criteria, collected to meet the specified number of samples, namely 110 cases. The variables in this study were urinary tract infection, anemia, maternal age, gestational age, education, parity, occupation, body mass index (BMI), history of caesarean section (CS), history of abortion, polyhydramnios, multiple pregnancies, history of bleeding, and premature rupture of membranes in preterm pregnancies. Anemia in pregnant women is determined by laboratory examination with hemoglobin (HB) criteria of 11 gr/dl. Urinary tract infection was measured by laboratory examination with criteria for a bacterial count of urine greater than 100,000/ml. Maternal age was divided into 2, namely age at risk (<20 years, >35 years) and not at risk (20-35 years). Gestational age was categorized into 2 groups, namely, 14mg-<34mg and 34-<37mg. Mother's education is divided into three categories: low (elementary, middle school), intermediate (high school), and high (Diploma, S1, S2, S3). Parity was assessed for primiparas and multiparas. Job variables are distinguished from working and not working. BMI measurement, normal (18.5-24.9 kg/m²), abnormal (<18.5 kg/m² or ≥25 kg/m²). In the variable history of CS, history of abortion, polyhydramnios, multiple pregnancies, history of bleeding, and PPROM were categorized as yes and no.

The medical records of each patient who was less than 37 weeks pregnant, both with and without PROM, were opened in order to collect data. The UGM Faculty of Medicine's ethics committee has granted KE/FK/0436/EC/2023 for this study's ethical approval. Statistical testing software was used to assess the data. The Chi-square test and logistic regression were used to evaluate the data.

3. RESULTS AND DISCUSSION

At the RSUP Dr. Sardjito Yogyakarta, preterm premature rupture of the membranes is a common occurrence. When cases were examined, it was discovered that many of them were accompanied by urinary tract infections and anemia. Preterm premature rupture of the membranes can be influenced by social, demographic, medical, obstetric, and behavioral factors [16].

3.1. Characteristic, anemia, urinary tract infections, and other factors' occurrence rates in the case and control groups

The case group's average age was 48 years old, with the youngest was 16 years old. Parity 3 was the highest parity. The control group discovered that the youngest was 18 and the oldest was 46. The case group's highest gestational age was 36 weeks and four days, while the control group's lowest gestational age was 24 weeks and five days. The highest value in maternal parity was 4.

According to data processing on a univariate analysis, the case group's urine bacteria count ranged from 1.9/ul, which was the lowest, to 47,581/ul, was the highest. In the case group, the lowest HB level was 7.3 mg/dl and the highest was 13.4 mg/dl. The control group's urine samples ranged in bacteria count from 0 to 36,173 per ul, with 0 being the lowest and 36,173 being the highest. In the control group, the HB levels ranged from 7.9 mg/dL to 15.5 mg/dL.

The Table 1 explains the univariate analysis and the percentage of maternal factors in all samples obtained in this study. The maternal factors studied were urinary tract infections, anemia, maternal age, gestational age, education, parity, occupation, body mass index, history of cesarean section, history of abortion, polyhydramnion, multiple pregnancies, bleeding history, and PPROM. The results of the univariate analysis are the percentages of each case group and control group.

Table 1. Univariate analysis

Maternal aspect factors		n	%
Urinary tract infection	Yes	120	54.5
	No	100	45.5
Anemia	Yes (HB<11gr/dl)	88	40
	No (HB≥11gr/dl)	132	60
Age	At risk, (<20 years, >35 years)	57	25.9
	Not at risk 20-35 years	163	74.1
Gestational age	14-<34 weeks	161	73.2
	34-<37 weeks	59	26.8
Education	Low (elementary, middle school)	37	16.8
	Intermediate (high school)	111	50.5
	Higher (Diploma, S1, S2, S3)	72	32.7
Parity	Primiparous (<2)	164	74.5
	Multiparous (≥2)	56	25.5
Jobs	Work	88	40
	Unoccupied	132	60
BMI before pregnancy	Normal (18.5-24.9 kg/m²)	111	50.5
	Abnormal (<18.5 kg/m²) or ≥25 kg/m²)	109	49.5
SC history	Yes	45	20.5
	No	175	79.5
Abortion history	Yes	51	23.2
	No	169	76.8
Polyhydramnion	Yes	8	3.6
	No	212	96.4
Multiple pregnancy	Yes	19	8.6
	No	201	91.4
Bleeding history	Yes	11	5
	No	209	95
PPROM	Yes	110	50
	No	110	50
	Total	220	100

3.2. Relationship of urinary tract infection, anemia and other factors with the incidence of preterm premature rupture of membrane

In this study, it was showed that the average age of pregnant women from all samples from the case group and the control group was 30.7 years, with the lowest age being 16 years and the highest being 48 years. The concentration of germs in urine ranged from 0 to 47,581/ul. In this study, pregnant women's lowest HB levels were 7.3 mg/d and their highest were 15.5 mg/d. The mother's gestational age ranges from 21 weeks to 36 weeks plus four days. Parity 4 has the highest parity. In cases of premature rupture of membranes in preterm pregnancies, the best time for delivery is recommended at 34 weeks, but this is controversial [17].

Preterm labor is thought to be caused by an infection [18] in which organisms produce collagenases, mucinases, and proteases that can weaken the amniotic and chorionic membranes and ultimately lead to membrane rupture. The significance of the association between urinary tract infection and premature membrane rupture in preterm pregnancy can be seen in the bivariate analysis carried out by Chi-square test. Based on the findings of statistical tests conducted on the variables related to urinary tract infections, values p-value=0.042<α (0.05), it can be deduced that there is a connection between urinary tract infections and the frequency of early membrane rupture in preterm pregnancy. This is consistent with the results of a study by Byonanuwe *et al.* This study found that a history of urinary tract infection was an independent predictor of premature rupture of membranes in pregnant women over 28 weeks' gestation, with a p-value=0.035 [19].

According to research by Addisu *et al.* claimed that urinary tract infection is one of the factors that contributes to premature membrane rupture [20].

A hemoglobin concentration of less than 11 g/dl is considered anemia [21]. It is clear from the analysis's results that there is a significant correlation between anemia and the incidence of preterm premature membrane rupture, and that there is a twofold risk of premature membrane rupture in the anemia variable, with a value p-value=0.009<0.05 and an OR value of 2.155. Anemia during pregnancy reduces the amount of hemoglobin in the tissues, which interferes with the substance's ability to transport oxygen throughout the body. For a healthy pregnancy, adequate iron intake is very important [22]. The amniotic membranes become more brittle due to low oxygenation, particularly in the amniotic tissue [15]. Anemia during pregnancy is also thought to increase the risk of having low birth weight kids [23]. This is in line with study results from Mahjabeen *et al.* who got p-value<0.05. So it can be concluded that there is a relationship between anemia and premature rupture of membranes [24].

Three external variables, namely gestational age, education, and parity, are significantly correlated with the incidence of premature rupture of membranes. Pregnant women with a gestational age of less than 37 weeks have a 1-4% chance of all pregnancies [25]. Given that variable gestational age was obtained in this study's bivariate analysis with chi squares test and had a p-value of 0.022 α< (0.05), it is possible to draw the conclusion that there is a significant correlation between gestational age and the likelihood of an early rupture of membranes in preterm pregnancy. This is consistent with the research conducted by Takele *et al.* [26] the results of the multivariate analysis showed an AOR: 3.28 (95% CI: 1.53, 7.02), meaning that pregnant women under 37 weeks had a 3.28-fold increased risk of PROM compared to those between 37 and 40 weeks. This research supports the findings of Diriba *et al.* study, which found a correlation between the mother's gestational age and the likelihood of an early membrane rupture with a p-value of 0.018<α (0.05) [16].

One of the risk factors for premature rupture of membranes is the educational status of the mother [3], [27]. Highly educated women are more aware of their own health and that of their families and tend to focus on diet and health checks during pregnancy [28]. A low level of education is always related to limited information and knowledge, the higher one's education, the higher one's understanding and knowledge of the information obtained [29]. It is intended that the mother will know more about the care of pregnant women the more educated she is, helping to avoid difficulties during pregnancy. Based on statistical tests, the bivariate analysis used in this study using Chi-square test, the education variable produced a p-value of 0.040 (<0.05). Therefore, it may be said that education and the likelihood of an early membrane rupture in a preterm pregnancy are related. High levels of knowledge help to prevent preterm pregnancies from having premature membrane rupture.

Multiple pregnancies put a mother at risk for premature rupture of membrane because of the uterus's poor vascularization, which causes the connective tissue of the amniotic membranes to become easily brittle and eventually break easily. Based on the results of the bivariate analysis statistical test using the chi square test, it was determined that the parity variable had a p-value of 0.044<α (0.05), leading to the conclusion that there is a substantial correlation between the incidence of early membrane rupture in preterm pregnancy and parity. Negative maternal and neonatal outcomes, such as prenatal depression, cesarean sections, and neonatal infant mortality, are more common in high-parity mothers [30].

Multiple pregnancies are one of the factors that cause premature rupture of membranes, caused by excessive stretching of the uterus that triggers rupture of the amniotic membranes. The results of bivariate analysis in this study show a p-value of 0.150>α (0.05), so it can be concluded that there is no significant relationship between multiple pregnancies and the incidence of premature rupture of membranes in preterm pregnancies. This is consistent with a study conducted by Zakiyyah *et al.* entitled Factors influencing the incidence of premature rupture of membranes in Probolinggo District, East Java, Indonesia, which states that there is no relationship between twin pregnancies and the incidence of premature rupture of membranes with a p-value of 0.435 [31].

While this is not in line with research conducted by Dewi *et al.*, which stated that there was a relationship between multiple pregnancies and premature rupture of membranes with a p-value of 0.01 (p<α=0.05) [32]. A healthy reproductive age range with a long lifetime is 20 to 35 [33]. Women over the age of 35 have a greater risk of fetal death and serious complications for the mother, which are more pronounced in mothers over 40 years of age [34]. Bivariate analysis in this study revealed a p-value of 0.124, indicating that there is no correlation between maternal age and the frequency of early membrane rupture in preterm pregnancy.

Working mothers have more activities; aside from being housewives, there are other professions that are carried out, so excessive physical activity is very likely to result in pregnancy complications, one of which is preterm premature rupture of membranes. The results of the bivariate analysis stated that for the occupational variable, the p-value was 0.491, where the value was <0.05, so it can be concluded that there is no relationship between work and the incidence of premature rupture of membranes in preterm pregnancy.

However, studies show that workload and working hours have a substantial impact on pregnant women's work stress levels [35]. Other external variables such as BMI, history of SC, history of abortion, and polyhydramnios on bivariate analysis have their respective p-values: variable BMI 0.418; variable history of SC=0.316; history of abortion =1.000; and polyhydramnios =1.000. So, it can be concluded that there is no significant relationship between BMI, history of SC, history of abortion, and polyhydramnios and the incidence of premature rupture of membranes in preterm pregnancy in RSUP Dr. Sardjito Yogyakarta in 2021 and 2022.

The Table 2 explains the bivariate analysis of maternal factors in all samples obtained in this study. The maternal factors studied were urinary tract infections, anemia, maternal age, gestational age, education, parity, occupation, body mass index, history of cesarean section, history of abortion, polyhydramnion, multiple pregnancies, bleeding history, and PPROM This bivariate analysis explains the relationship between maternal factors and the incidence of PPROM.

Table 2. Relationship of urinary tract infections, anemia and other factors related to incidence of preterm premature rupture of the membranes

Maternal aspects/Factors		Premature rupture of membranes				p-value
		Yes (Case)		No (Control)		
		n	%	n	%	
Urinary tract infection	Yes	52	47.3	68	61.8	0.042*
	No	58	52.7	42	38.2	
Anemia	Yes (HB<11gr/dl)	54	49.1	34	30.9	0.009*
	No (HB≥11gr/dl)	56	50.9	76	69.1	
Age	At risk, (<20 years, >35 years)	23	20.9	34	30.9	0.124
	Not at risk 20-35 years	87	79.1	76	69.1	
Gestational age	14-<34 weeks	88	80	73	66.3	0.022*
	34-<37 weeks	22	20	37	33.6	
Education	Low (elementary, middle school)	14	12.7	23	20.9	0.040*
	Intermediate (high school)	54	49.1	57	51.8	
	Higher (D1, D2, D3, S1, S2, S3)	42	38.2	30	27.3	
Parity	Primiparous (<2)	89	80.9	75	68.2	0.044*
	Multiparous (≥2)	21	19.1	35	31.8	
Jobs	Work	41	37.3	47	42.7	0.491
	Unoccupied	69	62.7	63	57.3	
BMI before pregnancy	Normal (18.5-24.9 kg/m²)	59	53.6	52	47.3	0.418
	Abnormal (<18.5 kg/m²) or ≥25 kg/m²)	51	46.4	58	52.7	
SC history	Yes	26	23.6	19	17.3	0.316
	No	84	76.4	91	82.7	
Abortion history	Yes	26	23.6	25	22.7	1.000
	No	84	76.4	85	77.3	
Polyhydramnion	Yes	4	3.6	4	3.6	1.000
	No	106	96.4	106	96.4	
Multiple pregnancy	Yes	13	11.8	6	5.5	0.150
	No	97	88.2	104	94.5	
Bleeding history	Yes	4	3.6	7	6.4	0.536
	No	106	96.4	103	93.6	
	Total	110	100	110	100	

3.3. Multivariate analysis of factors associated with preterm premature rupture of membranes

The final analysis used multivariate analysis the logistic regression analysis is shown in Table 3. The result showed that anemia, with a p-value of 0.007 and an OR value of 2.264, has the strongest correlation with the occurrence of early premature rupture of membranes. Compared to non-anemic moms, pregnant women with anemia had a 2.26-fold higher risk of early breakouts in preterm pregnancies. The main causes of morbidity in women are iron efficiency and anemia. This is a global health problem [36]. For the needs of the fetus, placenta, and increasing breast milk volume, additional iron is still needed. The amount remains constant throughout pregnancy at around 1,000 mg of iron. Throughout the first trimester, the amount is only 0.8 mg per day. The second and third trimesters increase significantly to levels of 6-7 mg per day [37]. Consuming iron tablets to prevent anemia has the effect of reducing the risk of premature birth [38]. One of the signs of premature birth is that it is preceded by premature rupture of the membranes. The prevalence of premature birth preceded by rupture of the membranes is around 30% [39].

The study was conducted at a major hospital, making it very challenging to collect research samples free of comorbidities. As a result, external variables that are unrelated to the incidence of premature rupture of membranes are very likely connected to research restrictions. The majority of the sample in this study consisted of comorbidly ill pregnant women who were referred by local hospitals.

Table 3. Final modeling of logistic regression analysis of factors associated to prematerm premature rupture of membranes

Variables	B	p-value	Exp(B)	95% CI	
				Lower	Upper
Anemia	0.772	0.007	2.264	1.238	3.783
Gestational age	0.769	0.017	2.159	1.150	4.051

4. CONCLUSION

From January 2021 to December 2022, anemia shows a statistically significant correlation with the frequency of early membrane rupture in preterm pregnancy at RSUP Dr. Sardjito Yogyakarta. Preterm Premature rupture of membrane is 2.3 times more likely to occur in pregnant women with anemia. Preterm premature rupture of memebrane is 2.1 times more likely in pregnant women who are less than 34 weeks along. Monitoring the prevention of anemia in pregnant women, which may be done since preparing for pregnancy, is very important because it is known that anemia has the most significant influence on the occurrence of early membrane rupture in premature pregnancies.

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