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MODIFIED FOAM STABILITY TEST (FS-50) AS PREDICTOR OF FETAL LUNG MATURITY IN PRETERM PREMATURE RUPTURE OF MEMBRANE PATIENTS GIVEN DEXAMETHASONE THERAPY

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Shake Test; Modified Foam Stability (FS-50); Lung Maturation; Preterm Premature Rupture of Membrane; Dexamethasone.

ABSTRACT
This study aims to determine the ability of the Modified Foam Stability (FS-50) test to predict fetal lung maturity in preterm premature rupture of membranes treated with Dexamethasone. The study sample included pregnant women with PROM at a gestational age of 24 to less than 34 weeks in the ER and Obstetrics Ward of Sanglah Central General Hospital, Denpasar. The patient underwent a vaginal speculum examination to collect fluid pooled in the vagina or from the outer cervical opening. Fluids are checked with the Modified Foam Stability (FS-50) test and graded from 0 to +4 to estimate fetal lung maturity. The first test was performed before Dexamethasone, followed by serial examinations at 12-hour intervals for 48 hours. Before dexamethasone injection, all patients got 0 scores as a baseline. There were statistically significant differences in FS-50 values before and after injection of the first, second, third, and fourth doses of Dexamethasone in PPROM patients. Fetal lung maturity was reached after the third dose of dexamethasone injection (36 hours after the first injection), characterized by an FS-50 value of > +3 and no asphyxia in the newborn. Spearman's rank analysis showed a significant correlation (p=0.005) between infants' maximum FS-50 value and asphyxia status. The FS-50 value > +3 is associated with the absence of asphyxia in infants born to PPROM patients who were given Dexamethasone for lung maturation. FS-50 can predict fetal lung maturity in preterm premature rupture of membranes given dexamethasone therapy.

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INTRODUCTION

Premature rupture of membranes (PROM) is a condition where the membranes rupture before delivery. PROM that occurs before 37 weeks of gestation is called preterm PROM or premature rupture of membranes (PPROM). The prevalence of PROM is quite large and tends to increase yearly. PROM at term occurs in about 6.46-15.6% of term pregnancies, while PPROM occurs in about 2-3% of singleton pregnancies and 7.4% of the total number of twin pregnancies (Prima & Putri, 2019). The data shows that 47.9% of infants with PPROM mothers may not survive, which aligns with a systematic review; the study reported that preterm labor accounts for as much as 75-80% of neonatal morbidity and mortality.

Preterm infant morbidity may impose physical, psychological, and economic burdens on babies, mothers, and families (Blencowe et al., 2012). Globally, approximately 11.1% of live births are preterm deliveries, with the rate of preterm labor in developing (low-income/middle-income) countries being higher than in developed (high-income) countries (Beck et al., 2010). In low-income/middle-income countries, more than 60% of preterm deliveries occur in Africa and South Asia (Sari et al., 2015). Indonesia is still in the top 10 countries with the highest estimated preterm birth rate (Rao et al., 2014).

Premature membrane rupture in preterm pregnancy significantly impacts perinatal outcomes, especially if the fetal lungs are immature (Niesłuchowska-Hoxha et al., 2018). One-third of PPROM will tend to get serious complications; the most common is fetal respiratory distress syndrome, where the incidence is higher in younger gestational age (Prima & Putri, 2019). Therefore, a lung maturity test is critical to predicting complications if the baby is delivered. The lecithin/sphingomyelin ratio (L/S ratio) is still the gold standard for lung maturity testing, but this test is relatively more expensive and challenging to perform (Ogbejesi & Tadi, 2020). Therefore, the shake test is more likely to be conducted serially because the results can be known quickly and easily. The modifications made by Edwards and Baillie (1973) proved to have the highest accuracy compared to the gold standard, with a method that is easier to perform and results that are easier to interpret. This modification uses an ethanol fraction of 0.50, hence the name FS-50 test (Edwards P, 1973).

Corticosteroid is one of the most important antenatal therapies before an anticipated preterm birth (Briceño-Pérez et al., 2019). Improved perinatal outcome was demonstrated in the women who received Dexamethasone. There was no increased risk of infection in the women or their infants where Dexamethasone was administered. Adequation of corticosteroids to women with PPROM has more advantages than disadvantages in developing countries (Pattinson et al., 1999). Expectant management within 14 days after PPROM is associated with poor neonatal outcomes. Decisions regarding an expectant strategy should be made carefully (Chaiyasit et al., 2017).

Therefore, this study aimed to know the ability of the Modified Foam Stability (FS-50) test to predict fetal lung maturity in PPROM treated with Dexamethasone. This study also aims to determine the time to reach fetal lung maturity after dexamethasone administration in PPROM regarding the FS-50 value and the incidence of asphyxia in the

fetus born and to determine the FS-50 test value associated with the incidence of asphyxia in infants born after administration of Dexamethasone.

METHODS

This study used a one-group pretest-posttest research design. The study sample was taken consecutively with a minimal sample size of 36, including pregnant women diagnosed with PROM at 24 weeks of gestation to less than 34 weeks with the following inclusion criteria: (1) Single pregnancy, (2) Live fetus according to USG, (3) Head presentation, (4) Diagnosed with PROM (positive litmus test), (5) Willing to participate in research and sign informed consent. Conditions included umbilical cord prolapse, rectal temperature >38oC, the mother with systemic disease (diabetes mellitus), pre-eclampsia and eclampsia, and a history of cervical surgery were exclusion criteria.

The sample is amniotic fluid for external uterine opening in PPROM patients aged 24-34 weeks. This is considered the pretest group. The treatment was lung maturation using Dexamethasone 6 mg via intramuscular injection every 12 hours for two days (total dose of 24 mg). Before the injection, the modified FS-50 test was performed, as the injection was performed every 12 hours four times; the FS-50 test results were obtained at 0, 12, 24, 36, and 48 hours as the post-test group. This research was conducted in the polyclinic, inpatient ward, and delivery room in the ER at Sanglah Central General Hospital, Denpasar, from January to December 2021.

This research data was processed using SPSS 26.0 version for Windows. Data analysis in this study included all data obtained. It was analyzed descriptively based on age, parity, BMI, and gestational age, the results presented in the distribution frequency table, and the data normality test with the Shapiro-Wilk test on all research samples. If the data distribution is expected, the decision is made using a paired sample T-test with $p < 0.05$, indicating a statistically significant value. If the data distribution is not normal, the decision is made using the Wilcoxon test with $p < 0.05$, indicating a statistically significant value.

RESULTS AND DISCUSSION

Demographic Characteristics

The mean age of the mother was 31 years, with the lowest maternal age being 20 years and the highest being 43 years. The sample characteristics based on parity obtained an average parity status of one, with the lowest value of zero parity and the highest value of parity of four. The mean gestational age was 31.46 weeks, with the most miniature gestational age at 26 weeks and the largest at 34 weeks. In the following variable, sample characteristics based on BMI obtained an average of 25.5 kg/m2, with the lowest value of 17 kg/m2 and the highest value of 41.4 kg/m2. Based on the maximum FS-50 value, an average of three was obtained, with the lowest score being one and the highest being four table 1.

Table 1. Characteristics of Research Samples

Variable	Total (%) (n=38)
Mother's age (tahun), mean±SD	31,39 ± 7,027
20-24	6 (15,8)
25-29	11 (28,9)
30-34	9 (23,7)
35-39	7 (18,4)
≥40	5 (13,2)
Parity, mean	1
0	17 (44,7)
1	10 (26,3)
2	8 (21)
3	3 (8)
Gestational age mean	31,46 ± 2,956
24-27	6 (15,8)
28-31	11 (28,9)
32-<35	21 (55,3)
BMI, mean	25,5
<18,5	1 (2,6)
18,5-22.9	6 (15,8)
23-24.9	11 (29)
25-29.9	18 (47,4)
≥30	2 (5,2)
FS-50 maximum value, mean	3,05
+1	4 (10,5)
+2	4 (10,5)
+3	15 (39,5)
+4	15 (39,5)
Conservative treatment success	
Born	26 (76,3)
Not	12 (23,7)
Delivery method	
Spontaneous	11 (42,3)
SC	15 (57,3)
Sex of the babies born	
Female	14 (53,8)
Male	12 (46,2)
Infant birth weight, mean±SD	1707,12 ± 589,587
<1000g	5 (19,2)
1000-<1500g	3 (11,5)
1500-<2000g	10 (38,5)
≥2000g	8 (30,8)

Asphyxia status	
Asphyxia	8 (30,8)
Not asphyxia	18 (69,2)

In terms of delivery outcomes, 12 patients (23.7%) with conservative treatment were successful, which means the baby was not born until the mother was discharged from the hospital (5 days of treatment), while 26 patients (76.3%) had advanced labor and were delivered before the completion of conservative treatment. Of the 26 patients who were born, 11 patients (42.3%) gave birth spontaneously, and 15 (57.3%) delivered by cesarean section. The sex of the babies born were 14 girls (53.8%) and 12 boys (46.2%). The average weight of babies born was 1,707.12 grams, with the lowest birth weight being 770 grams and the highest being 2,650 grams. In terms of the asphyxia status of infants, eight infants (30.8%) had asphyxia, and 18 infants (69.2%) did not have asphyxia.

Distribution of FS-50 Assessment Results and Delivery Outcomes by Time of Observation

At the beginning of the observation, before the first injection of Dexamethasone, no babies were born, and all samples (38 people/100%) got zero FS-50 scores. Within 12 hours after the first dexamethasone injection, no babies were born. On examination before the second dexamethasone injection, it was found that 33 patients (84.2%) got a positive FS-50 score of one, five patients (13.2%) got a positive score of two, and one patient (2.6%) got a positive score of three. As for the examination at 48 hours of 18 patients who have not given birth, one patient (5.6%) got a positive FS-50 score of two and four patients (22.2%) got a positive score of three, and 13 patients (72.2 %) got four positive values table 2.

Table 1. Distribution Of FS-50 Assessment Results And Delivery Outcomes By Time Of Observation

Observation t	Number Dexamethasone Injection	Number Babies Bo	Not Born (FS-50 value)					p
			0 (%	+1 (%	+2 (%)	+3 (%)	+4 (%)	
0 hours	-	0	38 (100)	0 (0)	0 (0)	0 (0)	0 (0)	
12 hours	I	0	0 (0)	32 (84,2	5 (13,2	1 (2,6	0 (0)	0,00
24 hours	II	7	0 (0)	0 (0)	13 (41,9	17 (54,8	1 (3,2	0,00
36 hours	III	6	0 (0)	0 (0)	3 (12)	18 (72)	4 (16	0,005
48 hours	IV	7	0 (0)	0 (0)	1 (5,6	4 (22,2	13 (72,2)	0,001
48-120 hours	-	6						

Distribution of Asphyxia Occurrence according to FS-50 Test Results Twelve Hours Prior

Within 12 hours after the first dexamethasone injection, seven babies were born. Four infants who scored +1 at the 12th hour all had asphyxia. Two infants who scored +2 all had asphyxia. At the same time, one baby who got a +3 value did not experience asphyxia.

Within 12 hours of the second dexamethasone injection, six babies were born. Two infants who scored +2 on the FS-50 test at the 24th hour all had asphyxia. Meanwhile, the four infants who scored +3 did not experience asphyxia. Within 12 hours after the third dexamethasone injection, seven babies were born. The four infants who scored +3 on the FS-50 test at the 36th hour did not have asphyxia. The other three infants who scored +4 also did not experience asphyxia. After giving the fourth dexamethasone injection until the fifth day of conservative treatment, there were six babies born. For infants who previously had a +3 on the FS-50 test at the 48th hour, two of those babies did not have asphyxia. The other four infants with a +4 also did not experience asphyxia table 3.

Table 2. Distribution Of The Occurrence Of Asphyxia According To The Results Of The FS-50 Assessment Twelve Hours Prior

Dexamethasone Post Injection do	Birth Time (hours since first injection	FS-50 valu 12 ho prior	Asphyxia Status		Total
			No asphyxia(%	Asphyxia (%)	
I	<24	+1	0 (0)	4 (100)	4 (57,1)
		+2	0 (0)	2 (100)	2 (28,6)
		+3	1 (100)	0 (0)	1 (14,3)
Total			1 (14,3)	6 (85,7)	7 (100)
II	24-36	+2	0 (0)	2 (100)	2 (33,3)
		+3	4 (100)	0 (0)	4 (66,7)
Total			4 (66,7)	2 (33,3)	6 (100)
III	36-48	+3	4 (100)	0 (0)	4 (57,1)
		+4	3 (100)	0 (0)	3 (42,9)
Total			7 (100)	0 (0)	7 (100)
IV	>48-120	+3	2 (100)	0 (0)	2 (33,3)
		+4	4 (100)	0 (0)	4 (66,7)
Total			6 (100)	0 (0)	6 (100)

Analysis of Maximum FS-50 Value Associated with Infant Asphyxia Status

In 26 infants born before the completion of conservative treatment, all infants who scored FS Max +1 and +2had asphyxia after birth. In contrast, none of the infants who scored FS-Max +3 and +4 had asphyxia after birth table 4.

Table 3. Spearman Rank Analysis Results For The Correlation Between The Maximum FS Value and Asphyxia Status of The Infants.

FS Max	Amount	Asphyxia Status (%)
+1	4	4(100)
+2	4	4(100)
+3	11	0(0)
+4	7	0(0)

The results of the Spearman rank analysis showed a significant correlation (p=0.005) between the maximum FS-50 value and asphyxia status in infants. This significant correlation is reasonably strong, with a coefficient value of -0.450. The negative value of the correlation coefficient also indicates a significant negative correlation, and the correlation between the two variables is not in the same direction. This means that the higher the maximum FS value, the less likely it is to experience asphyxia. In this study, a maximum positive FS value of three was shown to be associated with the absence of asphyxia in infants.

Demographic Characteristics

In this study, the highest maternal age was in the range of 25-29 years (28.9%), then aged 30-34 years old (23.7%), and 35-39 years old (18.4%). More than half of the patients were in the age range of 25-34 years old. These findings were supported by a similar study conducted by Mohan et al., who found that the most PPROM cases (50.1%) occurred in the 20-30 age group (Mohan et al., 2017). showed that the average age of mothers at risk of preterm birth was 27.±4.5 years (Rao et al., 2014). The study by Gafner et al. reported that the mean age of mothers with PPROM was 32 ± 5.98 years old, with a range of 20-45 years (Gafner et al., 2020). However, these findings were not supported by a study from Boskabadi which shows that PROM often occurs in maternal age less than 20 years or more than 35 years due to abnormal physiology of the amniotic membrane (Boskabadi & Zakerihamidi, 2019).

In this study, 44.7% of the sample had zero parity or were pregnant for the first time, 26.3% had one parity prior, and 21% had a history of two parities. In percentage, there is a tendency for the incidence of PPROM to decrease with increasing parity. There were no samples with a history of parity of more than three. Research conducted by Khade et al. also showed the same results; more PPROM occurred in multiparas (52%) than in primiparas (48%). The incidence of PPROM is often found in multiparous women because frequent pregnancies can affect embryogenesis so that the membranes formed will be thinner and break easily, and infection of the membranes is more likely to occur due to damage to the cervical structure from previous deliveries (Khade & Bava, 2018).

In this study, 55.3% of the samples were at the gestational age of 32-35 weeks, 28.9% were in the range of 28-31 weeks, and 25.8% were at 24-27 weeks. There is a tendency for the incidence of PPROM to increase along with the increasing gestational age. In highest number of cases (56.9%) with PPROM occurred near term (34-0 to 36-6 weeks).

The mean gestational age at the rupture of membranes was 34.1 weeks (Mohan et al., 2017). A retrospective study conducted in 2013-2016 in Israel by Gafner et al. reported a younger mean gestational age of mothers with PPROM, i.e., 18±3 weeks with a comprehensive range of 13-23 weeks, where the overall prognosis in the studied sample pregnancies showed that the closer to term, the more pregnancy outcomes, the better (Gafner et al., 2020).

The BMI of the sample in this study was 47.4% of the sample had a BMI of 25-29.9 (obesity grade I), 29% of the sample had a BMI of 23-24.9 (overweight), and 15.8% of the sample had a BMI of 18.5-22.9 (standard) WHO Western Pacific Region. There was a tendency for the incidence of preterm PROM to increase with increasing BMI in this study. This is supported by a study by Boskabadi & Zakerihamidi in 2019 which showed that PROM was more common in mothers with a low maternal body mass index (<19.8 kg/m2) (Boskabadi & Zakerihamidi, 2019). A meta-analytical of a total of 1,942 pregnant women with PPROM showed that maternal obesity was a risk factor for the occurrence of chorioamnionitis before the onset of labor. Obese women had a 60% increased complication risk (adjusted HR 1.6; 95% CI 1.1-2.1; p-value 0.008) (Hadley et al., 2019).

Asphyxia Status

In this study, 69.2% of infants born did not experience asphyxia, and the other 30.8% of infants had asphyxia. This is supported by research in 2013 by Azizah, which showed that at PROM for ≥ 12 hours, asphyxia was found in 44.7%, while PROM <12 hours with asphyxia found in 5.3%, with OR (odds ratio) 9.7 and p-value = 0.004, so that there is a significant difference between the duration of PROM (more than or less than 12 hours) and asphyxia (Syamsi & Zulala, 2021). A study by Syamsi and Zulala in 2020 in Yogyakarta on a total of 144 patients with PPROM showed that there was an association between a mother with PPROM and the incidence of neonatal asphyxia in neonates (p-value 0.024; CI 1.108-4.49; OR 2.232) and the coefficient of correlation 0.185. PPROM is associated with asphyxia because oligohydramnios can occur, which can compress the placenta so that the placenta will constrict (Syamsi & Zulala, 2021). Furthermore, the blood flow that carries maternal oxygen to the baby will be obstructed, and it can cause asphyxia or hypoxia.

Distribution of FS-50 Assessment Results and Delivery Outcomes by Time of Observation

At the 24th hours after the first dexamethasone injection, six of the seven infants born (85.7%) had asphyxia. At the 36th hour after the first injection of Dexamethasone, two of the six babies born (33.3%) had asphyxia, whereas 48 hours after the first dexamethasone injection, all babies born did not experience asphyxia. This shows that the longer the duration of corticosteroid administration, the lower the number of babies with asphyxia for 12 hours to 48 hours after corticosteroid administration, which proved statistically significant (p<0.05).

Several previous studies have tried to assess the association between the interval of corticosteroid administration at antenatal until delivery with neonatal outcomes. Results vary, ranging from 3-48 hours to achieve good neonatal outcomes, as shown by the absence of respiratory distress syndrome.

According to ACOG (2016), the current pulmonary maturation regimen requires 48 hours. It is known that treatment with corticosteroids for <24 hours has significantly reduced neonatal morbidity and mortality, so the first dose should still be given even though it may not complete the course of treatment. The threat of infection causes the pregnancy to be terminated early (<48 hours), where the risk of infection increases >12 hours. Research regarding the onset of lung maturation after administering this steroid is still rare, so the exact time is unknown.

Faizah found that giving Dexamethasone with various dosing (4-6 mg) every 12 hours for two days to pregnant women at risk of preterm delivery. After 48 hours, all samples showed good L/S ratio values greater than 2.0 (mature lungs). Babies born before 48 hours of corticosteroid exposure still needed resuscitation and ventilator support (Faizah et al., 2015).

Gross (1983) showed initial physiological effects six hours after the first dexamethasone injection. Glucocorticoids accelerate the maturation of the pulmonary surfactant system, namely the binding of glucocorticoids and their effect on phosphatidylcholine synthesis in rabbit fetal lung organ culture. Stimulation by corticosteroids was first observed after 12 hours of exposure. Choline incorporation increases linearly over 36 hours and then begins to stabilize; the removal of steroids after 24 hours prevents further stimulation.

Roberts et al. (2017) assessed 30 studies comparing antenatal corticosteroid treatment with placebo. They found a reduction of diseases associated with prematurity, including perinatal death, neonatal death, RDS, intraventricular hemorrhage (IVH), and systemic infections in the first 48 hours of life.

Administration of corticosteroids over 24 hours reduces the incidence of asphyxia. Ikegami showed that the benefit of corticosteroid administration is most excellent 2-7 days after the initial dose. Ideally, corticosteroids for lung maturation are timed to achieve maximum efficacy before delivery, which is 2-7 days after the first dose. Efficacy is considered complete more than 24 hours from the first dose and decreased after seven days.

Melamed assessed single neonates born between 24 0/7 and 33 6/7 weeks of gestation and admitted to a tertiary neonatal unit in Canada during 2010–2012 were obtained from the Canadian Neonatal Network. Their result showed that antenatal corticosteroids have maximum benefit when given between 1 and 7 days before birth (Melamed et al., 2015).

Elwany studied 52 pregnant women with singleton pregnancies at gestational age at risk of preterm delivery (24-34 weeks). They found that antenatal administration of Dexamethasone to women at risk of preterm pregnancy will improve fetal and uteroplacental blood flow 24 hours after administration of this drug. Significant differences in umbilical Doppler, MCA, uterine artery, and aorta compared before 24 hours of

dexamethasone administration. Administration of betamethasone or Dexamethasone is continued even if labor is expected to occur within 24 hours after injection, which administration of these drugs is considered most effective when labor occurs 24 hours from the onset of administration.

Norman showed that administration interval to birth >48 hours is associated with reduced severe neonatal brain injury. An interval of 18-36 hours is associated with a reduction in mortality of more than 50%. Administration of antenatal corticosteroids as early as 3 hours earlier has resulted in an estimated 26% reduction in mortality. Assuming a causal relationship between antenatal corticosteroid timing and mortality, Simulations of antenatal corticosteroids administered three hours before delivery to infants who did not receive antenatal corticosteroids showed an estimated 26% reduction in mortality. It can be concluded that antenatal corticosteroids may be effective even if administered only a few hours before delivery. Therefore, infants of pregnant women who are at risk for preterm labor may benefit from its use (Norman et al., 2017).

Distribution of Asphyxia Occurrence according to FS-50 Assessment Results Twelve Hours Prior

In this study, all infants with asphyxia had an FS-50 score measured twelve hours earlier with a value below +3. On the other hand, all infants with a positive FS-50 score of three or more at 12 hours before the observation did not have asphyxia. This shows that the higher the FS-50 value, the better the neonatal outcome. The FS-50 examination can predict the occurrence of asphyxia, with a positive minimum value of three as a predictor that the baby to be born will not have asphyxia.

Spearman's rank analysis showed a significant relationship (p=0.005) between infants' maximum FS-50 value and asphyxia status. This significant relationship has a relatively strong correlation with a coefficient value of -0.450.

The negative value of the correlation coefficient also indicates a significant negative relationship; that is, the relationship between the two variables is not in the same direction. This means that the higher the maximum FS value, the less likely it is to experience asphyxia. In this study, the FS-50 value of more than or equal to +3 was shown to be associated with the absence of asphyxia in infants.

Analysis of Maximum FS-50 Value Associated with Infant Asphyxia Status

This study found a significant correlation (p = 0.005) between the maximum FS-50 value and asphyxia status in infants, where a maximum FS value of more than positive three was shown to be associated with the absence of asphyxia in infants.

A fetal maturity test was one of the methods to anticipate the RDS, which is done on amniotic fluid obtained by amniocentesis or collected from the vagina in membranes that have ruptured. Cao reported that the conventional test for predicting fetal lung maturity is based on the exchange of lipids between the developing lung and amniotic fluid that is assessed by the amount of surfactant in the amniotic fluid. Measuring the lecithin/sphingomyelin (L/S), ratio by this layer chromatography was a conventional

method for measuring surfactants in amniotic fluid. A high L/S ratio is associated with increasing gestational weeks as the sphingomyelin concentration remains relatively constant, while lecithin concentration increases during late pregnancy (Cao et al., 2020).

The foam stability index test evaluated the surfactant in amniotic fluid. The more excellent foam stability forms when the amniotic fluid is combined with ethanol and shaken, the more surfactant in amniotic fluid. Usually, shake tests only provide a probable index of the functional activity of surfactants in amniotic fluid with only qualitative information, either positive (presence of stable foam) or negative (absence of stable foam). With the quantitative interpretation of the FS-50 test, we could give a better prediction of whether the test result indicates normal fetal respiratory status or there is a risk of respiratory distress. Hence, we can predict and counsel patients on the pregnancy outcome (Alvarado & Arce, 2016).

CONCLUSION

There was a statistically significant difference in FS-50 values between prior and after the first, second, third, and fourth doses of dexamethasone injection in preterm premature rupture of membranes. This study found that fetal lung maturity was achieved after the third dose of dexamethasone injection (36 hours after the first injection) in preterm premature ruptured membranes, which was characterized by FS-50 values > +3, and none of the babies born experienced asphyxia. FS-50 value less than +3 is associated with asphyxia in infants born to preterm premature rupture of membranes.

BIBLIOGRAFI

Alvarado, A., & Arce, I. (2016). Metabolic functions of the lung, disorders and associated pathologies. *Journal of Clinical Medicine Research*, *8*(10), 689.

Beck, S., Wojdyla, D., Say, L., Betran, A. P., Merialdi, M., Requejo, J. H., Rubens, C., Menon, R., & Van Look, P. F. A. (2010). The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bulletin of the World Health Organization*, *88*, 31–38.

Blencowe, H., Cousens, S., Oestergaard, M. Z., Chou, D., Moller, A.-B., Narwal, R., Adler, A., Garcia, C. V., Rohde, S., & Say, L. (2012). National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *The Lancet*, *379*(9832), 2162–2172.

Boskabadi, H., & Zakerihamidi, M. (2019). Evaluation of maternal risk factors, delivery, and neonatal outcomes of premature rupture of membrane: A systematic review study. *Journal of Pediatrics Review*, *7*(2), 77–88.

Briceño-Pérez, C., Reyna-Villasmil, E., & Vigil-De-Gracia, P. (2019). Antenatal corticosteroid therapy: Historical and scientific basis to improve preterm birth management. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *234*, 32–37.

Cao, Z., Liu, J., Xie, X., Zhan, S., Song, W., Wu, S., Sun, Z., Dong, Y., Tang, G., & Liu, Y. (2020). Lipidomic profiling of amniotic fluid and its application in fetal lung maturity prediction. *Journal of Clinical Laboratory Analysis*, *34*(4), e23109.

Chaiyasit, N., Romero, R., Chaemsaithong, P., Docheva, N., Bhatti, G., Kusanovic, J. P., Dong, Z., Yeo, L., Pacora, P., & Hassan, S. S. (2017). Clinical chorioamnionitis at term VIII: a rapid MMP-8 test for the identification of intra-amniotic inflammation. *Journal of Perinatal Medicine*, *45*(5), 539–550.

Edwards P, J. & B. (1973). A simple method of detecting pulmonary surfactant activity in amniotic fluid. *South African Medical Journal*, *47*(43), 2070–2073. https://doi.org/https://journals.co.za/doi/10.10520/AJA20785135_30068

Faizah, R. N., Yahya, M., & Abadi, A. (2015). DEXAMETHASONE STUDY FOR PRENATAL LUNG MATURATION ON LECITHIN/SPHINGOMYELIN RATIO IN WOMEN AT RISK OF PRETERM BIRTH. *Folia Medica Indonesiana*, *51*(1).

Gafner, M., Borovich, A., Gimpel, A., Peled, Y., Meshulam, M., & Krissi, H. (2020). Risk factors and maternal outcomes following preterm premature rupture of membrane in the second trimester of gestation. *Archives of Gynecology and Obstetrics*, *301*, 1207–1212.

Hadley, E. E., Discacciati, A., Costantine, M. M., Munn, M. B., Pacheco, L. D., Saade, G. R., & Chiossi, G. (2019). Maternal obesity is associated with chorioamnionitis and earlier indicated preterm delivery among expectantly managed women with preterm premature rupture of membranes. *The Journal of Maternal-Fetal & Neonatal Medicine*, *32*(2), 271–278.

Khade, S. A., & Bava, A. K. (2018). Preterm premature rupture of membranes: maternal and perinatal outcome. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, *7*(11), 4499–4506.

Melamed, N., Shah, J., Soraisham, A., Yoon, E. W., Lee, S. K., Shah, P. S., & Murphy, K. E. (2015). Association between antenatal corticosteroid administration-to-birth interval and outcomes of preterm neonates. *Obstetrics & Gynecology*, *125*(6), 1377–1384.

Mohan, S. S., Thippeveeranna, C., Singh, N. N., & Singh, L. R. (2017). Analysis of risk factors, maternal and fetal outcome of spontaneous preterm premature rupture of membranes: a cross sectional study. *Int J Reprod Contracept Obstet Gynecol*, *6*(9), 3781–3787.

Niesłuchowska-Hoxha, A., Cnota, W., Czuba, B., Ruci, A., Ciaciura-Jarno, M., Jagielska, A., Wójtowicz, D., Kierach, R., Dąbrowski, K., & Sidorowicz, M. (2018). A retrospective study on the risk of respiratory distress syndrome in singleton pregnancies with preterm premature rupture of membranes between 24+ 0 and 36+ 6 weeks, using regression analysis for various factors. *BioMed Research*

International, *2018*.

Norman, M., Piedvache, A., Børch, K., Huusom, L. D., Bonamy, A.-K. E., Howell, E. A., Jarreau, P.-H., Maier, R. F., Pryds, O., & Toome, L. (2017). Association of short antenatal corticosteroid administration-to-birth intervals with survival and morbidity among very preterm infants: results from the EPICE cohort. *JAMA Pediatrics*, *171*(7), 678–686.

Ogbejesi, C., & Tadi, P. (2020). *Lecithin Sphingomyelin Ratio*.

Pattinson, R. C., Makin, J. D., Funk, M., Delport, S. D., Macdonald, A. P., Norman, K., Kirsten, G., Stewart, C., Woods, D., & Moller, G. (1999). The use of dexamethasone in women with preterm premature rupture of membranes-A multicentre, double-blind, placebocontrolled, randomised trial. *South African Medical Journal*, *89*(8).

Prima, A., & Putri, K. (2019). *Jurnal Saintika Medika The Relationship Of Leukocyturia On The Incidence of Prominent Rupture of The Membrane in Preterm Pregnancy at the General Hospital of The University of Muhammadiyah Malang*.

Rao, C. R., de Ruiter, L. E. E., Bhat, P., Kamath, V., Kamath, A., & Bhat, V. (2014). A case-control study on risk factors for preterm deliveries in a secondary care hospital, southern India. *International Scholarly Research Notices*, *2014*.

Sari, I. M., Adisasmita, A. C., Prasetyo, S., Amelia, D., & Purnamasari, R. (2015). *Effect of premature rupture of membranes on preterm labor : a case-control study in Cilegon , Indonesia*. 1–6.

Syamsi, E. Y., & Zulala, N. N. (2021). Premature Rupture of Membrane (PROM) Increasing Asphyxia Neonatorum Risk. *International Conference on Health and Medical Sciences (AHMS 2020)*, 232–234.