Research Article

Threatened Preterm Labor: Which are become Preterm Labor?

Ancaman Persalinan Preterm: Mana yang menjadi Persalinan Preterm?

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Abstract

Objective: To show about characteristics of subject, fetal fibronectin, vaginal pH, cervical length of women with threatened preterm labor, and which are become preterm labor? Preterm labor is occurs most often in 20 weeks gestation to less than 37 weeks gestation. This condition is concerned about Obstetric problem and associated with significant neonatal morbidity and mortality.

Methods: This study used the design of case *control* where preterm pregnant women who become research subjects divided into two groups with threat and without the threat of pre-term labor. Fetal fibronectin , vaginal pHand cervical length than in both groups were evaluated as a risk factor for preterm labor. Mann-Whitney test , Wilcoxon test and Chi-squared test were used as statistical tests with a confidence level of 95%.

Results: A total of 86 preterm pregnant women involved in this study with an average age 30.5 ± 6.25 (group threat) 32.16 ± 5.25 (non-threatening). Comparison of fetal fibronectin (p = 0.005), vaginal PH(p <0.001) and length of the cervix (p <0.001) between the two groups showed a significant difference. A total of 8 subjects of the 43 in the group of pregnant women with the threat pretem labor experiencing preterm labor .

Conclusions: The size of a short cervical length, an increase in the pH of the vaginal secretions and increased levels of fetal fibronectin is a clinical indicator for screening during pregnancy to assess the risk of a preterm labor.

Keywords: cervical length, fetal fibronectin, preterm labor , vaginal pH of the secretions.

Abstrak

Tujuan: *Persalinan preterm adalah persalinan yang terjadi padausia kehamilan 20 hingga kurang dari 37 minggu. Kondisi ini merupakan permasalahan yang sangat mengkhawatirkan dalam bidang kebidanan dan dikaitkan dengan morbiditas dan kematian neonatal yang signifikan. Evaluasi dan skrining terhadap berbagai faktor risiko terjadinya ancaman persalinan preterm adalah hal terpenting dalam mencegah berbagai komplikasi yang mungkin timbul.*

Metode: *Penelitian ini menggunakan desain case control di mana perempuan hamil preterm yang menjadi subjek penelitian terbagi menjadi dua yakni kelompok dengan ancaman dan tanpa ancaman persalinan preterm. Fetal fibronectin, pH sekret vagina dan panjang serviks dibandingkan diatara kedua kelompok sebagai faktor resiko ancaman persalinan preterm. Mann-Whitney test, Wilcoxon test dan Chi– squared digunakan sebagai uji statistik dengan tingkat kepercayaan 95%.*

Hasil: *Sebanyak 86 perempuan hamil preterm terlibat dalam penelitian ini dengan rerata usia 30,5 ± 6,25 (kelompok ancaman) 32,16 ± 5,25 (tanpa ancaman). Perbandingan Fetal fibronectin (p=0,005), pH sekret vagina (p<0,001) dan panjang serviks (p<0,001) antar kedua kelompok menunjukkan adanya perbedaan yang bermakna. Sebanyak 8 subjek dari 43 pada kelompok perempuan hamil pretem dengan ancaman persalinan preterm yang mengalami persalinan preterm.*

Kesimpulan: *Ukuran panjang serviks yang pendek, peningkatan pH sekret vagina dan peningkatan kadar fetal fibronectin merupakan indikator klinis untuk skrining selama kehamilan guna menilai risiko terjadinya persalinan preterm.*

Kata kunci: *fetal fibronectin, persalinan preterm, Ph vagina, panjang cerviks.*

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INTRODUCTION

Preterm labor is labor that occurs at a gestational age of 20 to less than 37 weeks were marked by regular uterine contraction followed by thinning and dilation of the cervix.[1]It is estimated that as much as 0.5 % of deliveries occur before the third trimester. Preterm childbirth can cause a variety of medical and social problems, fetuses born prematurely require special care and have a greater risk of abnormalities or health problems both short and long term. Short-term abnormalities that often occur are RDS (Respiratory Distress Syndrome), intra/periventricular hemorrhage, NEC (Necrotrizing Entero Cilitis), bronchopulmonary displacement, sepsis, and patent ductus arteriosus. Furthermore, long-term abnormalities that can occur include neurological disorders such as cerebral palsy, retinopathy, mental retardation, and neurobehavioral dysfunction can also occur. This condition can lead to low quality of human resources in the future will come. Besides premature baby care also requires sophisticated and expensive medical technology (for example Neonatal Intensive Care Unit / NICU, Surfactant) thereby increasing the burden of health financing.[2,3]

In an effort to reduce perinatal mortality and morbidity, assessment of risk factors is an important thing to do in every pregnancy. Theoretically, various risk factors have been identified in the form of a history of previous preterm labor, alcohol consumption, smoking, a history of trauma and psychosocial disorders. However, these risk factors are not sufficiently objective in determining the risk of preterm labor, so other specific examinations are needed to improve the accuracy of the predictions.[4]

One risk factor that can be measured objectively using Ultrasonographic modalities is cervical length.[5]In addition, Fetal Fibronectin (FFN) levels are also a predictor for preterm labor The level of vaginal acidity is closely related to the growth of vaginal microbiota and is a major predisposing factor for infection. Bacterial vaginosis is one of the most common causes that cause preterm labor.[6-8]

Based on the above background, researchers are interested in conducting studies to assess differences in fetal fibronectin levels, pH of vaginal secretions, and cervical length in preterm pregnant women with and without the threat of preterm labor.

METHODS

The design of this study case control where preterm pregnant women who become research subjects divided into two groups with threats and without the threatened preterm labor.This research was conducted in the delivery room of the Dr. Zainoel Abidin (RSUDZA) Banda Aceh from February 2018 to November 2019.

Subjects were selected as research subjects based on the following inclusion criteria: Pregnant women with gestational age 24 - < 37 weeks, Pregnant women with the threat of premature parturition (case group), Pregnant women without the threat of prematureparturition (controlgroup), Pregnantwomenwithsinglefetuses living *intrauterine* and Subjects thatwere not selected were subject to research based on the following exclusion criteria: premature rupture of membranes, cervical dilatation ≥ 3 cm, having sex within 24 hours, placental ablution, placenta previa, and vasa previa, cervical cerklase, diabetes mellitus, diabetes mellitus, hypertension, heart disease, kidney and liver, fetus with anomalies, intrauterine growth retardation.

Fetal fibronectin measurement is done by taking a specimen from the posterior fornix then measured using a fetal fibronectin rapid test, measurement of vaginal pH by taking a vaginal specimen and then measured using a Paper Ph strip while the length of the cervix is measured using transvaginal ultrasonography. Fetal fibronectin, the pH of the vaginal secretions and cervical length than diatara both groups as a threat risk factor preterm labor. Mann-Whitney test, Wilcoxon test and Chi-squared test were used as statistical tests with a confidence level of 95%.

RESULTS

Based on the results of data collection for 10 months at the RSUD dr. Zainoel Abidin Banda Aceh obtained data of 86 women with preterm pregnancies, of which 43 were threatened preterm labor and 43 without preterm labor. Data distribution of research subjects is presented in the following table.

Table1. General Characteristic of Research

Variable	The threatened preterm labor	
	Threat (+) (n=43)	Threat (-) (n=43)
Age		
< 20	2 (4.7)	0
20 – 35	32 (74,4)	31 (72,1)
> 35	9 (20.9)	12 (27.9)
Gravida		
G1	15 (34.9)	9 (20.9)
G2	7 (16.3)	9(20.9)
G3	6 (14)	8 (18.6)
G4	7 (16.3)	11 (25.6)
G5	5 (11.6)	5 (11.6)
G6	1 (2.3)	1 (2.3)
G7	1 (2.3)	0
G8	1 (2.3)	0
Parity		
P0	16 (37.2)	12 (27.9)
P1	9 (20.9)	8 (18.6)
P2	5 (11.6)	10 (23.3)
P3	6 (14)	11 (25.6)
P4	4 (9.3)	2 (4.7)
P5	2 (4.7)	0
P6	0	0
P7	1 (2.3)	0
Abortion		
A0	38 (88.4)	31 (72.1)
A1	4 (9.3)	11 (25.6)
A2	1 (2.3)	0
A3	0	1 (2.3)
Gestational Age (weeks)		
27 – 28	1 (2.3)	0
28 – 29	6 (14)	4 (9.3)
29 – 30	2 (4.7)	3 (7)
30 – 31	4 (9.3)	5 (11.6)
31 – 32	5 (11.6)	4 (9.3)
32 – 33	3 (7)	2 (4.7)
33 – 34	6 (11.6)	0
34 – 35	5 (11.6)	9 (20.9)
35 – 36	12 (27.9)	16 (37.2)
Occupational status		
Employed	9 (20.9)	6 (14)
Unemployed	34 (79.1)	37 (86)
Level of education		
Primary school	1 (2.3)	4 (9.3)
Middle school	2 (4.7)	3 (3.5)
High school	25 (58.1)	18 (41.9)
Diploma	4 (9.3)	5 (11.6)
Associate's Degree	3 (7)	1 (2.3)
Bachelor's Degree	8 (18.6%)	12 (60%)

The table above shows the characteristics of the subjects in this study based on age, gestational history, parity, history of abortion, age of pregnancy, Occupational status and level of education. Women diagnosed with threatened preterm labor are mostly found in the 20-35 age group and have these following characteristics; gravida 1, parity 0, abortus 0 whereas women without threatened preterm labor are mostly gravida 4, parity 0 and abortus 0.

Table 2. Data on the distribution of preterm labor threats

Variable	The threatened preterm labor	
	Threat (+) (n=43)	Threat (-) (n=43)
Age (years)	30.5 ± 6.25	32.16 ± 5.25
Cervix Length	2.32 ± 0.27	3.43 ± 0.23
Vaginal PH	5.05 ± 0.61	4.23 ± 0.44
Fetal fibronectin (positive negative)	8/35	0/43

The table above presents research demographic data based on age, cervical length, Vaginal PHand *fetal fibronectin*. The difference between the two groups is not far apart namely by a difference of 1,66 years. The length of a woman's cervix with the threatened preterm laboris shorter than that of the non-threatening group and has a more alkaline vaginal PH. In contrast to preterm pregnant women without the threatened preterm laborwho all showed negative *fetal fibronectin*, 8 subjects with the threatened preterm laborshowed positive *fetal fibronectin* levels.

Table 3. Data distribution of preterm labor events

Variable	The incidence of preterm labor	
	Labor (n = 8)	Not labor (n = 35)
Age (years)	29.38 ± 6.58	30.77 ± 6.25
Cervix Length	1.77 ± 0.13	2.44 ± 0.06
Vaginal PH	5.63 ± 0.51	4.91 ± 0.56
Fetal fibronectin (positive / negative)	8/0	0/35

Data on the incidence of preterm labor is presented in the table above. Preterm pregnant women who experienced preterm labor (8 people) had an average age of 29.38 years with shorter cervical length compared to women who did not experience preterm labor. vaginal pHof women with preterm labor is more basic and all show positive fetal fibronectin levels.

DISCUSSION

Preterm labor is the process oflabor that occurs at gestational age 20 to 37 weeks.[9] The condition begins with uterine contractions before the age of 37 weeks that causes the cervix thins and opens. If the threatened preterm laborcan not be stopped, the conditions that will end up as preterm labor (preterm birth).[9]

Preterm labor is a very worrying problem in the field of midwifery and is associated with significant neonatal morbidity and mortality.

At present, identifying women at high risk for preterm labor is a big challenge.[10,11]

Several other retrospective studies testing fetalfibronectin using an enzyme - linked immunosorbent assay report that the risk of preterm labor can be proportionally detected by taking specimens in cervicovaginal fluid.[12]

The study also reported the same thing where there was a significant relationship between a fetal fibronectin levels and the threatened preterm laborin preterm pregnant women (p = 0.005). Furthermore it was also known that there was a relationship between fetal fibronectin levels in preterm women and the threatened preterm labor to the incidence of preterm labor (p <0.001). Our data support previous studies which concluded that fetalfibronectin testing could be predictor of preterm labor in high-risk asymptomatic women and mild risk pregnant women.[12,13]Moreover, this examination shows consistent sensitivity and specificity values in different study populations.[14]

Fetal fibronectin measurement in cervical fluid is a good predictor of spontaneous preterm labor in symptomatic and asymptomatic women after 22 weeks of gestation. FFN can be detected in cervical and vaginal fluid before 20 weeks of gestational age and very low levels are found after 22 weeks (<50 ng / Ml). A level of ≥50 ng / Ml after 22 weeks has been associated with an increased risk of preterm labor.[15] Such tests already become qualitative tests that produce results either positive or negative based on the value of the threshold of 50 ng / mL[16]

Fetal fibronectin diffuses diffuctively in the fetal membrane from the amnion to the decidua, providing structural support and adhesion of the fetal membrane to the uterine lining. FFN in cervicovaginal secretion has been used as a clinical marker of preterm labor. However, the exact pathogenesis between fetal fibronectin and preterm labor is not yet fully known. Many studies have hypothesized that fetal fibronectin in cervical fluid indicates disruption of the fetal-maternal link and the release of fetal matrix molecules into the vagina. Studies others have reported that proteolytic degradation of FFN leads to the activation of MMP-9 in the domain specialized immune cells that infiltrate the membrane zone were weak.[17]

In addition to fetal fibronectin examination, measurement of cervical length is also a good modality for assessing the risk of preterm labor. Short cervix is associated with an increased risk of preterm labor in several studies. The same thing was also proven in this study where there was a significant relationship between the length of the cervix of a preterm pregnant woman against the threatened preterm laborand was directly related to the incidence of preterm labor. Clinical trial research conducted by Hassan et al reported that the risk of preterm labor decreased in women with short cervix who were given vaginal progesterone therapy.[18]This is also a reference for universal screening using ultrasound in women with short cervix.[19,20]

The combination of fetal fibronectin examination and cervical length measurement to identify women at high risk for preterm labor has been proven by studies conducted on 132 subjects of pregnant women at high risk of preterm labor. Concluded that positive fetal fibronectin examination and cervical length ≤25 mm were associated with 53% of preterm labor events at <37 weeks' gestation.[21]

A different matter was reported that quantitative examination of cervicovaginal fluid fibronectin and cervical length measurements of nulliparous women before 37 weeks' gestation showed a low prediction rate of preterm labor accuracy. They concluded that the combination of the two examinations had a low sensitivity and an estimated score.[22] However, despite its low diagnostic significance, cervical length measurement is the only effective predictor of follow-up intervention. Screening of cervical length measurements has been done universally in patients who will receive progesterone therapy which decreases the incidence of preterm labor in women with cervical length <20 mm or less.[23]

Another factor that is associated with the threat and incidence of preterm labor at gestational age <35 weeks is intrauterine infection. Bacterial Vaginosis (BV) is one of the most common causes of infection. Bacterial vaginosis is a modification of the reduced amount of normal vaginal flora (lactobacilli) which plays a role in increasing vaginal pH.[24] These modifications also increase the colonization of various anaerobic or other facultative microorganisms such as Gardenerellavaginalis, Prevotellasp, Bacteroides sp, Mobiluncus sp, gram-negative coccus bacteria and genital mycoplasms (Mycoplasma hominis and Ureaplasmaurealyticum).[25]

A large population meta-analysis (20,000 women) from 18 studies evaluating vaginal PH associated with BV concluded that BV doubled the risk of preterm labor before 37 weeks'

gestation.[26]Preterm labor in women with vaginal PH> 5 is seen 3 times more than PH <5 with an odd ratio of 3.06).[27] Study reported that PH <5 not only correlated with an increased risk of preterm labor, but also reported a moderate correlation between increased vaginal pH and short cervix.[28]

The same thing we got in this study where there is a significant relationship between the vaginal PHand the threatened preterm labor. The mean vaginal PHwith the threatened preterm labor was 5.05, while women without the threatened preterm laborhad a vaginal PH4.[23] In addition, we also report that there is a significant relationship between Vaginal PHand the incidence of preterm labor in women with threats. PH examination of vaginal secretions is a modality that has good accuracy in examining preterm labor in advanced pregnancy.[29] Other studies also prove that the increase in vaginal PHcan be used as a predictor to identify the risk of preterm labor so that it can be used as a modality to prevent the occurrence of preterm labor.[30]

The cause of preterm labor is multifactorial. The pathophysiology of this condition involves various clinical indicators such as proinflammatory cytokines in amniotic fluid in the second trimester, fetal fibronectin expression in cervicovaginal mucus, cervical shortening on ultrasound examination and increased maternal salivary estriol. Changes in the level of vaginal acidity due to various processes are also an important factor which shows a significant relationship to preterm labor with fetal body weight <2.000 grams or less than 1.500 grams. Increasing the vaginal PHat the age of 16-22 weeks of pregnancy has a close relationship with the reduction in cervical length thereby increasing the risk of preterm labor.[30]

CONCLUSION

Short cervical length, an increase levels of vaginal pH and increased levels of fetal fibronectin is a clinical indicator for screening during pregnancy to assess the risk of a preterm labor.

SUGGESTION

Further research needs to be done that checks the level of fetal fibronectin quantitatively , a further research is needed with a higher number of research subjects.

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