Original Article

Prevalence of Amniotic Fluid Sludge in Low-Risk Pregnant Women of Preterm Delivery

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Background: Amniotic fluid sludge (AFS) has been demonstrated in cases of intrauterine infection, one of the causes of preterm labor. Therefore, AFS is used as a predictor of preterm labor.

Objective: To determine prevalence of AFS in low-risk pregnant women and diagnostic performance of AFS for screening of preterm delivery in low-risk cases of preterm delivery.

Materials and Methods: Prospective descriptive study was conducted in low-risk pregnant women of preterm delivery who attended the antenatal care clinic in Rajavithi Hospital at gestational age (GA) 16 to 24 weeks between May 1, 2016 and October 31, 2017. All subjects were examined by transvaginal ultrasound to demonstrate AFS and then followed until delivery.

Results: Prevalence of AFS in all cases was 72/330 cases (21.8%). Premature delivery occurred in AFS positive and AFS negative were 3/72 (4.2%) and 22/258 (8.5%), respectively. Baseline characteristics were similar except mean BMI, and type of contraception. Mean GA at delivery was the only significant different obstetrical outcome. Diagnostic performances of AFS for screening low risk pregnant women for spontaneous preterm delivery less than 37 weeks of gestation had sensitivity of 12.0%, specificity of 77.4%, accuracy of 77.4%, positive predictive value of 4.2% and negative predictive value of 91.5%.

Conclusion: Prevalence of AFS in low-risk pregnant women of preterm delivery was 21.8%. AFS is not sensitive for screening of preterm delivery in low-risk cases.

Keywords: Amniotic fluid sludge, Preterm labor, Pregnancy

J Med Assoc Thai 2019;102(Suppl.4):40-4
Website: http://www.jmatonline.com

Preterm labor is an important problem worldwide associated with neonatal morbidity and mortality[1-5]. Nowadays, specific causes of preterm labor[1-7] are still unknown but some studies suggested that intrauterine infection may be one of the causes[1-7]. Several complications such as respiratory distress syndromes, intraventricular hemorrhage, periventricular leukomalacia and necrotizing enterocolitis, could have occurred in the preterm babies[8].

Amniotic fluid sludge (AFS) defined as a dense aggregate material within the amniotic fluid cavity close to cervical os during transvaginal ultrasound during 1st and early 2nd trimester[1,4,9-11] (Figure 1). Highly echogenic material is similar to calcification[11,12]. Sludge associated with impending preterm birth, histologic chorioamnionitis and microbial invasion of the amniotic cavity (MIAC) with spontaneous preterm labor with intact membranes[4,12]. AFS was demonstrated in the intrauterine infected cases[6,12]. So AFS was used as a predicted of preterm labor by some clinicians[1-5,10].

Recently, small number of papers regarding to AFS-predicted preterm labor were reported[1-6,10-12]. Most studies performed in cases with high risk for preterm labor[1,3,11,12] and some with preterm labor[5,10]. Only one Brazilian study conducted both high and low risk for preterm labor[13]. So the present study was conducted to determine prevalence of AFS in low risk pregnant women and diagnostic performance of AFS for screening of preterm delivery in low-risk cases.

Materials and Methods

A prospective cross-sectional study was performed in pregnant women whose gestational age (GA) between 16 to 24 weeks attending at antenatal care clinic (ANC), Rajavithi Hospital (RH) between May 1, 2016 and October 31, 2017 after approval from Rajavithi Ethics Committee (No. 59063). Written, informed consent was obtained from every subject. Exclusion criteria are high risk preterm features, dead fetus *in utero*, congenital malformation, multifetal pregnancy, previous preterm labor, history of cervical cerclage and preterm premature rupture of membranes.

Each case was examined with one operator. After voiding and lying in lithotomy position, subjects were inserted with transvaginal probe, (5 to 7 MHz, Voluson S6, GE. Healthcare (Zift, Austria). AFS was defined as dense

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How to cite this article: Kovavisarach E, Jongfuangprinya K. Prevalence of Amniotic Fluid Sludge in Low-risk Pregnant Women of Preterm Delivery. J Med Assoc Thai 2019;102(Suppl.4):40-4.

Figure. 1 Amniotic fluid sludge (AFS).

aggregates of particulate matter in the amniotic fluid closed to the internal cervical os finding from ultrasound (Figure 1). Only single AFS was examined in each case. All cases were follow-up until delivery.

Data included demographic characteristics such as maternal age, GA, cervical length (CL), parity, body mass index (BMI), GA at delivery, neonatal birth weight, Apgar score, presence of AFS were recorded. They were analyzed with the IBM SPSS statistics version 22.0. A percentage, Chi-square test, Fisher's exact test and independent t-test were used to assess prevalence and adverse outcomes of amniotic fluid sludge in low risk pregnant and their obstetrical outcomes. A *p*-value of <0.05 was considered statistically significance.

The sample size was calculated by the following formula[14]

$$n = \frac{Z^2_{\alpha/2}\, p\ (1\text{-}p)}{d^2}$$

n = Sample size; p = prevalence of preterm labor in amniotic fluid sludge positive patients = 0.226[7]; $Z_{\alpha/2} = 1.96$ (statistic significant $\alpha = 0.05$); d = 20% of p = 0.2 x 0.226 = 0.046

$$n = \frac{1.96^2 \text{ x } 0.23\text{x } (1 - 0.23)}{0.046^2}$$

n = 322 cases

Results

Three hundred and thirty cases were included and AFS were visualized in 72 cases (21.8%). Twenty-two out of 258 cases in the AFS negative group were premature deliveries (8.5%) while 3 out of 72 cases in the AFS positive group were premature deliveries (4.2%). Baseline characteristics are shown in Table 1. Mean body mass index (BMI) and type of contraception were significant difference between groups ($p = 0.005$ and 0.042, respectively). Table 2 shows the obstetrical outcomes. Only mean GA at delivery is significant difference ($p<0.041$). When AFS was used as a screening test for screening of preterm delivery in low-risk cases of preterm delivery, it had a sensitivity of 12%, specificity of 77.4%, accuracy of 77.4%, positive predictive value (PPV) of 4.2% and negative predictive value of 91.5%.

Discussion

Prevalence of AFS in low risk pregnant women in the present study was 21.8%. Marked variations of AFS 1 to 33%[1-4,10,11,13] were previously reported. Different characteristics such as high or low risk for preterm delivery may denominate a quite different prevalence.

AFS was reported as a significant risk factor for spontaneous preterm delivery in asymptomatic cases at risk of spontaneous preterm delivery[1,3,11]. Prevalence of AFS of the high risk cases in those studies were 16.7 to 23.5%[1,3,11]. Espinoza et al[4] reported the significant higher presence of AFS (22.6%) in the preterm labor with intact membranes as compared with 1% in the uncomplicated term pregnancies. Only single paper[10] reported that AFS is not a significant risk factor of preterm in patients with cervical cerclage. There was no significant difference in mean GA at delivery between presence and absence AFS, (36.4±4.0 vs. 36.8±2.9 weeks, $p = 0.530$)[10]. Different populations especially low risk for preterm delivery in the present study, while high risk for preterm delivery in the other studies, may explain the different results[1,3].

Strengths of the present study were prospective design and all the cases were follow-up until delivery. Based on our knowledge, the present study reported the maximum number of AFS (72 cases) while the other studies included AFS cases varied from 5 to 66 cases[1-5,10,11,13,15]. Limitation of the present study was low prevalence of preterm delivery; that could be explained as all the participants were low risk for spontaneous preterm delivery. So the prevalence of preterm deliveries was quite low in every group such as 4.2%. 8.5%, and 7.6% in AFS positive, AFS negative and both groups, respectively.

Similar studies in high risk for preterm labor, prevalence of preterm delivery in AFS negative group varied from 17.3% to 27.0%[1,3,11] while those in the AFS positive groups varied from 62.2% to 80.0%[1,3,11]. When AFS was analyzed according to the delivery outcome, the presence of AFS occurred such as higher in the preterm labor compared with those in term groups (22.6% vs. 1.0%)[4]. Because the study was not designed to determine the relationship of AFS and preterm delivery and the sample size was calculated for the prevalence of AFS in low-risk pregnant women. So the relationship of AFS and preterm delivery was difficult to

Table 1. Baseline characteristics of patients

Characteristic	Total (n = 330)	AFS negative (n = 258)	AFS positive (n = 72)	*p*-value
Race				0.500[a]
Thai	300 (90.9)	236 (91.5)	64 (88.9)	
Other	30 (9.1)	22 (8.5)	8 (11.1)	
NICU				1.000[b]
Yes	14 (4.2)	11 (4.3)	3 (4.2)	
Parity				0.185[a]
Nulliparous	84 (25.5)	70 (27.1)	14 (19.4)	
Multiparous	246 (74.6)	188 (72.9)	58 (80.6)	
Age				0.738[b]
19 to 34 years	52 (15.8)	41 (15.9)	11 (15.3)	
>35 years	273 (82.7)	212 (82.2)	61 (84.7)	
<18 years	5 (1.5)	5 (1.9)	0 (0.0)	
Mean ± SD	36.28±4.27	36.11±4.45	36.64±3.47	0.360[b]
Median (min-max)	36 (15 to 45)	36 (15 to 45)	37 (21 to 45)	
BMI (kg/m^2)				0.048*[a]
<18	17 (5.2)	11 (4.3)	6 (8.3)	
18 to 25	219 (66.4)	166 (64.3)	53 (73.6)	
>25	94 (28.5)	81 (31.4)	13 (18.1)	
Mean ± SD	23.64±4.21	23.95±4.34	22.30±3.30	0.005*[c]
Median (min-max)	23 (15.0 to 43.7)	23.3 (15.0 to 43.7)	22 (16.6 to 34.0)	
Contraception				0.840[a]
Yes	75 (22.7)	58 (22.5)	17 (23.6)	
Type of contraception				0.042*[b]
OCP	63 (84)	50 (86.2)	13 (76.5)	
DMPA	7 (9.3)	3 (5.2)	4 (23.5)	
Condom	5 (6.7)	5 (8.6)	0 (0.0)	
Underlying disease				0.430[a]
Yes	67 (20.3)	50 (19.4)	17 (23.6)	
TVS CL (cm)				0.218[b]
<2.5	1 (0.3)	0 (0.0)	1 (1.4)	
≥2.5	329 (99.7)	258 (100.0)	71 (98.6)	
Mean ± SD	4.00±0.90	4.00±0.90	4.00±0.90	0.993[c]
Median (min-max)	3.8 (2.0 to 7.6)	3.8 (2.5 to 7.6)	3.9 (2.0 to 6.5)	

Value are represented as number (percent), * = Statistical significant at $p<0.05$
a = The *p*-value for Chi-square test; b = The *p*-value for Fisher's exact test; c = The *p*-value for Independent t-test
AFS = amniotic fluid sludge

determine.

According to the diagnostic performance for screening of preterm delivery in low-risk cases of preterm delivery, sensitivity and PPV were very poor (12.0% and 4.2%, respectively) while only NPV was very good (91.5%) and both specificity and accuracy (77.4% and 77.4%, respectively) were fair. Adanir I et al[11] reported the diagnostic performance of AFS to identify cases with high risk for spontaneous preterm delivery before 37 weeks of gestation in the high risk for spontaneous preterm delivery as follows; sensitivity of 37.5%, specificity of 90.0%, PPV of 67.0% and NPV of 73.0%.

In both studies, the present study and Adanir's study had quite low sensitivity (12.0% and 37.5%, respectively). Adanir's study had very good specificity (90.0%) and fair NPV (73.0%). While our study had very good NPV (91.5%) and fair specificity (77.4%). The different result might be explained by different characteristics of the subjects such as low risk for spontaneous preterm delivery and Thai race in the present study while high risk and Turkish race in Adanir's study. However, it was quite difficult to determine the diagnostic performance because of low prevalence of preterm delivery and only present study and Adanir analyzed the result for diagnostic performances. Then AFS should not be used for screening high risk case for spontaneous preterm delivery because of its low sensitivity 12.0 to 37.5%.

Even though, mean BMI and GA at delivery were significant different statistics, there were no clinical significance because the very small difference of mean BMI (22.3 and 23.3 kg/m^2) and term GA at delivery (38.4 and 38.0 weeks) in the AFS positive and AFS negative groups, respectively.

Conclusion

Prevalence of amniotic fluid sludge was 21.8%

Table 2. Outcomes of pregnancy

Characteristics	Total (n = 330)	AFS negative (n = 258)	AFS positive (n = 72)	*p*-value
Sex				0.473[a]
Male	171 (51.8)	131 (50.8)	40 (55.6)	
Female	159 (48.2)	127 (49.2)	32 (44.4)	
PPROM				0.721[a]
Yes	41 (12.7)	31 (12.3)	10 (13.9)	
Mode of delivery				0.939[b]
Normal labor	136 (41.2)	107 (41.5)	29 (40.3)	
Forceps extraction 2	2 (0.6)	2 (0.8)	0 (0.0)	
Vacuum extraction 3	3 (0.9)	3 (1.2)	0 (0.0)	
Cesarean section	189 (57.3)	146 (56.6)	43 (59.7)	
GA at delivery				0.041[c]
Mean ± SD	38.14±1.87	38.00±1.91	38.40±1.14	
Median (min-max)	38.1 (27 to 41)	38.0 (27 to 41)	38.2 (35 to 41)	

Value are represented as number (percent), * = Statistical significant at $p<0.05$
[a] = The *p*-value for Chi-square test; [b] = The *p*-value for Fisher's exact test; [c] = The *p*-value for Independent t-test
PPROM = preterm premature rupture of the membrane, AFS = amniotic fluid sludge

Table 3. Preterm labor association with amniotic fluid sludge

Characteristics	Term (n = 305)	Preterm (n = 25)	Crude OR	Adjusted OR	95% CI	*p*-value
Sludge						0.266
No sludge	236 (91.5)	22 (8.5)	2.14	2.58	0.49 to 13.69	
Sludge	69 (95.8)	3 (4.2)				

Value are represented as number percent, Statistical significant at $p<0.05$
OR = odds ratio; CI = confidence interval

Table 4. Diagnostic performance of amniotic fluid sludge

Characteristics	Term (n = 305)	Preterm labor (n = 25)	Total (n = 330)
Sludge			
Positive	69 (95.8)	3 (4.2)	72 (100.0)
Negative	236 (91.5)	22 (8.5)	258 (100.0)

Value are represented as number (percent)

- Sensitivity	=	$\frac{3}{3+22}$	= 12.0% (8.0 to 16.0)
- Specificity	=	$\frac{236}{69+236}$	= 77.4% (76.4 to 78.4)
- Accuracy	=	$\frac{3+236}{3+22+69+236}$	= 77.4% (75.4 to 79.4)
- Positive predictive value	=	$\frac{3x100}{72}$	= 4.2% (3.2 to 5.1)
- Negative predictive value	=	$\frac{236x100}{258}$	= 91.5% (90.5 to 92.4)

in the low-risk pregnancy and it is not sensitive for screening of preterm delivery in low- risk cases of preterm delivery.

What is already known on this topic?

Small number of papers regarding to AFS-predicted preterm labor reported diagnostic performance of AFS for

screening of preterm delivery in low-risk cases of preterm delivery.

What this study adds?

Prevalence of amniotic fluid sludge was 21.8% in the low-risk pregnancy. Amniotic fluid sludge is not sensitive for screening of preterm delivery in low-risk cases of preterm delivery.

Acknowledgements

The authors wish to thank Assistant Professor Somboon Sornsukonrat, Head of the Department of Obstetrics and Gynecology, Rajavithi Hospital, for his kind permission to report the study. Finally, we would like to thank Rajavithi Hospital for funding this research.

Potential conflicts of interest

The authors declare no conflict of interest.

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