ORIGINAL ARTICLE

The Use of Fetal Fibronectin and Vaginal pH as new Laboratory Markers for Detection of Preterm Delivery in Iraq

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ABSTRACT

Background: In Iraq, vaginal fFN and vaginal pH are not used in clinical settings as biomarkers to evaluate the preterm delivery.
Aim: To evaluate the use of vaginal fFN test and measuring of vaginal pH in early prediction of preterm delivery.
Methods: 37 pregnant women were enrolled in this study, 23 of them were patients group with suspected preterm delivery, while the remaining 14 pregnant women were a control group. Vaginal speculum and vaginal swab were used to help in collecting the specimen, the cervicovaginal secretions, then after, these secretions were used for fFN testing by a fFN Rapid Test cassette /all test company/ China and to measure the vaginal pH by vaginal pH Rapid test /all test company/China. The demographic and clinical data were obtained by a questionnaire.
Results: the result of the current study showed that 12(52.2%) of patients' group were positive for vaginal fFN, while the other 11(47.8%) of this group were negative; all pregnant women in the control group were negative for vaginal fFN. Sixteen (70%) of patients' group and 10(71%) of control group have an elevated vaginal pH. PTL was the outcome in 12/12 (100%) of patients positive for fFN and in 4 patients negative for fFN, while all control group were completed full term labor. In the patients' group, fetal death or health problems are more frequent in positive fFN (7/12(58%)) than in fFN negative (0/11(0%)). There is no statistical differences regarding ages, clinical features, and type of delivery in fFN positive or negative and in high vaginal pH or normal pH.
Conclusions : Vaginal fFN is an important biomarker for predicting PTL and fetal health, while high vaginal pH is a common finding in most of pregnant women whether they are at risk of PTL or normal pregnancy. The age of pregnant women, clinical features, and the type of delivery have no relation to vaginal fFN positivity or to high vaginal pH.
Keywords: Fibronectin, vaginal pH, pregnancy, preterm labor

INTRODUCTION

Preterm birth, also known as preterm labor (PTL), is defined as birth before 37 weeks of gestation; it is a significant public health issue[1]. Despite advances in obstetric care, approximately 1 in 10 infants is born preterm[2]. About 30% of preterm births are medically indicated due to maternal or fetal causes, such as preeclampsia and intrauterine fetal growth restriction. The remaining 70% are spontaneous preterm births, which are attributed to preterm premature rupture of membranes or spontaneous onset of PTL[3,4].

Fetal fibronectin (fFN) is a glycoprotein produced by the chorion, and it is believed that fFN have a role in implantation and placental attachment of fertilized egg to the uterus. Normally, fFN can be detected in cervical and vaginal secretions prior to 20 weeks' gestation, but the presence of fFN in these secretions after 22 weeks of gestation usually indicates that a disruption of the utero placental interface has occurred. fFN can be detected in cervical and vaginal secretions using a specific monoclonal antibody assay. The presence of fFN has become the basis for screening women for possible preterm labor[1,2,3].

In addition to fFN, vaginal pH level can be another indicator for PTL. Normal vaginal pH is between 3.8 and 4.5, which is moderately acidic. Having a vaginal pH higher than 4.5 puts a pregnant woman at risk for PTL because of vaginal infection, notably, bacterial vaginosis (BV) which is a lower genital tract bacterial infection characterized by change in normal vaginal flora and replacement by vaginosis-associated anaerobic microorganisms. BV is a leading cause of many undesirable fetal outcomes including premature birth and premature rupture of fetal membranes[5,6]. In this aspect, screening of vaginal pH may be a good diagnostic tool for PTL[7].

The use of fetal fibronectin and measuring vaginal pH as laboratory markers to predicate abortion or preterm delivery has not been used previously in Iraq (including Kurdistan region). The aim of this study is to apply new laboratory techniques, testing fetal fibronectin and vaginal pH, for the prediction of abortion and preterm delivery.

METHODS

Two study groups were enrolled, a patient group involved pregnant women (n=23) at risk of preterm delivery (threatened PTL), and a second control group. The control group (n=14) was subdivided into two subgroups: seven healthy pregnant women and seven pregnant women with conditions not associated with threatened premature delivery. The control group is age matched with patient group.

Any patient was entering the emergency department of Maternal Teaching Hospital/Sulaimani city and diagnosed, as suspected case of premature labor by the gynecologists was included in patient study.

The study was done in Maternity Teaching Hospital/ Sulaimani city/Kurdistan Region of Iraq. This prospective study extended from December 2018 until April 2019.

The methods include three major parts: fFN in vaginal sections, vaginal pH and a questionnaire for data collection, which include demographic data such as age,

occupation, residency and clinical data involved features, related to PTL including vaginal bleeding, abdominal pain, back pain, pelvic pain, and vaginal secretion.

Detection of fFN in cervicovaginal secretion was done by, qualitative immunochromatographic test, rapid test cassette./ALL TEST Company/China

The vaginal pH is measured by Vaginal pH Rapid Test Panel (vaginal Swab) /ALL TEST Company/China, it is a semi-quantitative detection of pH in female vaginal swab specimen.

The cervicovaginal secretion is obtained using a sterile polyester swab from the posterior fornix of the vagina during a sterile speculum examination or, if no vaginal fluid is visible, the sample may be taken from the cervix.

Version 16 SPSS was used for data entry and analysis. Chi-square test (X2) and fisher's exact test were applied to test the association between categorical variables. P value of ≤ 0.05 was considered as statistical significant. An approval from the scientific committee of the Sulaimani Technical College of Health/Sulaimani Polytechnic University was taken and a signed informed consent was obtained from pregnant women participating in this study.

RESULTS

The results revealed that 12/23 (52.2%) of patient's group were positive to fFN protein test while the remaining 11/23 (47.8%) were negative; none of the control group (n=14) were positive for fFN protein, the results were statistically significant (P value equals 0.0009) (Fig.1)

The current study showed that 16 (70%) of patients' group have an elevated vaginal pH with mean of pH=5.9, and 10 (71%) of control group also have an elevated in pH level with mean of pH=5.2, the results were statistically not significant (P value equals 1.0000) (Table 1).

The age range of pregnant women in patients' group was between 18 to 41 years old with mean age equal to 29 years old; 8 (66.7%) of positive fFN patients are with ages below 30 years while the other 4 (33%) positive fFN patients have ages equal or above 30 years. These results showed no statistical significance when compared to patients (n=11) with negative fFN patients, p value equals to 1.0000; similar results for vaginal pH was recorded, p value =0.3707 (Table 2).

More than two thirds (22/37) of patients were living in rural areas of Sulaimani city, 26/37 of them were housewives while the rest were with different occupations. Five clinical features were screened among patients group: abdominal pain, backache, pelvic pain, vaginal bleeding, and vaginal discharge. None of these clinical features was significantly differ between positive fFN patients and negative fFN patients (Table 3).

The results of this study showed that preterm labor is more frequent in patients with positive fFN in vaginal secretion (12/12) than in patients without (4/11), these differences are statistically significant (Table 4).

Three of pregnant women in patients' group with positive fFN were complaining from fetal death before delivery, another four pregnant women were gave birth to babies with health problems, none of such condition were present in patients with negative fFN, the differences were statistically significant (p value <0.05) (Table 5).

The preterm delivery and the presence of borne babies with health problems (or dead babies) in patients' group is more frequent than in control group, and the differences are statistically significant; both groups have no statistical differences regarding both types of deliveries, vaginal and cesarean deliveries (Table 6).

Fig. 1: Prevalence of fFN among study groups

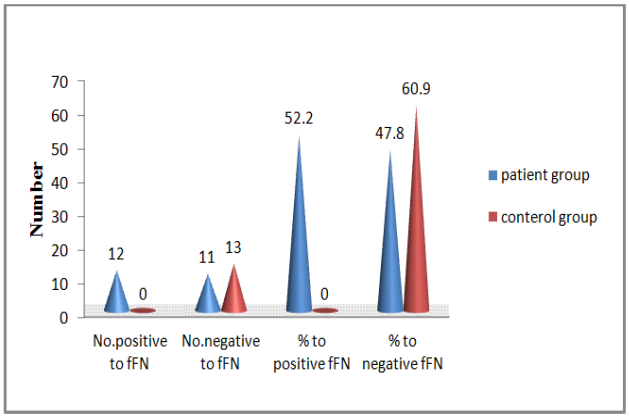

Table 1: The frequency of vaginal pH among study groups

Group	Patients Group	Control Group
Normal pH Frequency%	7 (30%)	4 (29%)
Elevated pH Frequency%	16(70%)	10(71%)
Normal pH Frequency% with PTL	1/7 (14.3%)	0
Elevated pH Frequency%with PTL	7/16 (43.8%)	0

Table 2: The age distribution of patients' group according to vaginal fFN and pH results

Age	<30	≥30
Positive fFN Frequency%	8(66.7%)	4(33.3%)
Negative fFNFrequency%	8(72.7%)	3(27.3%)
High vaginal pHFrequency%	7(58.3%)	5(41.7%)
Normal vaginal pH Frequency %	9(81.8%)	2(18.2%)

Table 3: The frequency of clinical features in patients' group

Clinical features	Patients group Frequency%		P value
	Positive fFN (n=12)	Negative fFN (n=11)	
Abdominal pain	8	8	1.000
Backache	8	7	1.000
Pelvic pain	0	0	1.000
Vaginal bleeding	4	0	0.0932
Vaginal discharge	9	8	1.000

Table 4: The outcome of pregnancy in patients' group

Type	Patients' group positive for fFN (n=12)	Patients' group negative for fFN (n=11)	P value
Preterm labor	12	4	0.0013*
Term labor	0	7	
Normal vaginal delivery	12	8	0.0932
Caesarian section	0	3	

** Significant*

Table 5: The health status of borne babies in patients' group

Type	Patients' group positive for fFN (n=12)	Patients' group negative for fFN (n=11)
Normal baby	5	11
Baby with health problems	4	0
Dead fetus	3	0

*P Value 0.0046** **Significant*

Table 6: The outcome of pregnancy in patients' and control groups

Type	Patients' group (n=23)	Control group(n=14)	P value
Preterm labor	16	0	<0.0001*
Term labor	7	14	
Normal vaginal delivery	20	12	1.000
Cesarean section	3	2	
Normal baby	16	14	0.0309*
Baby with problems	4	0	
Dead fetus	3	0	

** Significant*

DISCUSSION

In this study, we tested pregnant women for the possible beneficial testing of those who are liable to preterm labor through investigating the presence of fFN protein in vaginal secretions and semi-quantitative measurement of vaginal pH. According to our knowledge, it is the first study in Kurdistan region that tries to detect fFN and measure vaginal pH in cervicovaginal secretion of pregnant women that at risk of PTL.

Among pregnant at risk of PTL, the fFN was positive in 52.2% and all of these positive women suffered spontaneous preterm birth, thus 100% of pregnant women with positive fFN had PTL, which reflect the importance of this test in predicting PTL in pregnant women at risk to perform measures to prevent prematurity whenever possible. On the other side, only 36.3% of pregnant women who are at risk of PTL but negative for fFN got PTL, this reflect the usefulness of testing fFN test; similar results were obtained in a systematic review study done by Kiefer, et al[8], while the results of Bastek JA, et[9] were against ours.

In normal pregnancy, the vaginal pH is usually less than 4[10]; the current study should that vaginal pH is elevated more than the normal in nearly 70% of PTL risk group and 71% of control group. In PTL risk group the women with higher than normal vaginal pH were more prone to spontaneous preterm labor than those with normal pH in the same group. Thus, it is better to measure the vaginal pH during pregnancy to patients at risk of PTL, Gleeson RP, et al [(11)], got results that are in accordance to ours; the presence of high vaginal pH in 70% of control group rises the attention regarding the health status of apparently normal women and the possibility of asymptomatic infections[12].

In the current study, the women with positive fFN are at higher risk of fetal morbidity and mortality than those with negative fFN in cervicovaginal secretion, this reflect the importance of this test during pregnancy. As most of pregnant women who suffer premature labor without obvious cause, it is better to include the fFN as a screening test to predict PTL at least for those at risk.

The age of patients with risk of PTL, their type of delivery, and their clinical features were not a significant factor for positive fFN or for high vaginal pH.

CONCLUSION

Vaginal fFN is an important biomarker for predicting PTL and fetal health while high vaginal pH is recorded in most of pregnant women whether they are at risk of PTL or normal pregnancy needs to be analyzed for the possible cause of which PTL is one of them. The age of pregnant women, clinical features, and the type of delivery have no relation to vaginal fFN positivity or to high vaginal pH. In this aspect, it is recommended to use the fetal fibronectin rapid test for diagnosis of preterm delivery health care facilities in Sulaimani city, and response measures to fFN will help in reduction of fetal morbidity and mortality.

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