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EVALUATION OF VAGINAL FLUID B-HCG FOR THE DIAGNOSIS OF PREMATURE RUPTURE OF MEMBRANES

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ABSTRACT

Objectives: The aim of this study is to determine the role of quantitative level of β-HCG in vaginal fluid in diagnosis of premature rupture of membranes. **Design:** Prospective case control randomized study. **Setting:** El-Hussein University and Sohag Teaching Hospitals from May 2016 – November 2016. **Materials and Methods:** A total of 150 pregnant women in gestational age between 20 and 40 weeks were included in this study and were divided into three groups: *group I* (conformed PROM), *group II* (suspected but unconfirmed PROM) and *group III* (intact membrane group). All patients underwent ultrasonographic examination for gestational age and amniotic fluid index (AFI) calculation, sterile speculum examination for detection of amniotic fluid pooling and Nitrazine paper testing followed by vaginal fluid sampling for measurement of quantitative level of β-HCG by immulite method. **Results:** The mean vaginal fluid hCG levels in group I, group II and group III were 455.80 ± 119.27, 113.24 ± 58.38 and 24.75 ± 15.15 mIU/mL respectively in which the difference was statistically significant (P<0.001). With hCG cut-off value ≥62 mIU/ml, the sensitivity100%, specificity98%, positive predictive value 100%, and negative predictive value 99% with diagnostic accuracy of 99.9% in confirming PROM. **Conclusion:** β-hCG titer was significantly higher in cases with definite PROM. Consequencely, vaginal fluid hCG can be used as an easy, rapid, reliable and non-invasive test for confirming the diagnosis of PROM and can be used as a adjunctive test in an equivocal cases.

KEYWORDS: β-human chorionic gonadotropin, premature rupture of membranes.

INTRODUCTION

Premature rupture of membranes PROM is the rupture of membranes before the onset of labour while (PPROM) is defined as rupture of fetal membranes before onset of labor at less than 37 completed weeks of gestation.[1] PROM can occur at any gestational age even at 42 weeks gestation.[2] It has previously been reported to occur in 8-19% of term pregnancies and 2-25% of all pregnancies.[3]

Premature rupture of membranes is a significant problem that faces every obstetrician. The high neonatal mortality rate associated with PROM is contributed to a number of obstetric complications, the most important of which are; chorioamnionitis and preterm delivery. It accounts for one-third of preterm births.[4] Other complications are cord prolapse, fetal distress, pulmonary hypoplasia and limb deformities.[5]

Diagnosis of PROM can be done by history of gush of fluid per vagina that moists vulval pads and several studies have been conducted to find a definite, easy, noninvasive and reliable diagnostic test for PROM.[6]

Human chorionic gonadotropin is a glycoprotein produced exclusively by syncitio-trophoblasts in the placenta. As pregnancy progress, mean level of β-hCG in maternal circulation increase to approximately 54,000mIU/mL at 8-12 weeks of gestation. It then declines rapidly reaching a nadir at approximately 20 weeks of gestation; this nadir is maintained at approximately 12,000 mIU/mL during the third trimester. β-hCG is present in AF as well as maternal blood and urine, at concentrations ranging from approximately 2000 to 70,000mIU/mL.[7]

Because hCG is secreted by cervical glands; a certain level should be present in vaginal fluid. Therefore, hCG levels will be measured and compared in the vaginal fluid of normal pregnant women and pregnant women with PROM. It is will be hypothesized further that levels of hCG in vaginal fluid would be a good diagnostic indicator of PROM, if these values were low compared with those in amniotic fluid (AF).[8]

PATIENTS AND METHODS

This study is a prospective randomized case-control study which was done to evaluate the diagnostic potential of human chorionic gonadotrophin (HCG) measurement in vaginal fluids as an indicator of ruptured fetal membranes (PROM).

This study was designed on pregnant women attending El-Hussein University and Sohag Teaching Hospitals in gestational age between 20 and 40 weeks from May 2016 to November 2016.

A total of 150 pregnant women were included in the study and were divided into three groups:

Group I: PROM group in which pregnant women with definite history of premature rupture of membranes confirmed by speculum examination and Nitrazine paper test *(n =50).*

Group II: Suspected PROM group *(n = 50).*

Group III: Pregnant women with no history of rupture of membranes as a control group *(n = 50).*

Inclusion criteria

Group I in which age from 18-35 years, gestational age between 20-40 wks and absence of regular uterine contractions for all groups while definite history of premature rupture of membranes, pooling of AF in the posterior vaginal fornix during sterile speculum examination and positive Nitrazine paper test for group (I) only while history suspecting PROM for group (II) only and no history of PROM with negative Nitrazine paper test for group (III) only.

Exclusion criteria

Patients at less than 20 week, presence of any amount of spontaneous vaginal bleeding to be excluded, and pregnancies complicated by oligohydramnios, intrauterine growth restriction (IUGR), fetal anomalies and post-term pregnancies.

Study Procedures

After taking an informed consent, history taking and general examination, all patients were subjected to a speculum examination.

AF pooling with or without vulsalva maneuver was noted. Their history of coitus within 48 hrs of admission was recorded. Infectious discharge and bleeding during the speculum examination were also recorded. All patients underwent ultrasonographic examination for gestational age determination and amniotic fluid index (AFI) calculation.

Sample Collection

Patients lied in lithotomy position in good illumination. Sterile vaginal examination using a sterile Cusco speculum was done then vaginal fluid sampling was done. Cases must give history suggestive of PROM but no fluid seen by inspection. After confirming with a negative Nitrazine test, the absence of AF pooling and no bloody discharge in the posterior fornix, the vaginal fornix was irrigated with 3-ml of sterile saline inside a 5-ml syringe by which vaginal washing was subsequently aspirated from the posterior fornix.

The sample was centrifuged at 1500 revolutions per minute for 5 minutes at room temperature, and the supernatant was stored at -20°C until assay.

Concentration of β-HCG in the samples will measured with immulite method in the same laboratory and by the same technique.

RESULTS

Table (1): Comparison between groups according to characteristics of the patients.

	Group I	Group II	Group III	ANOVA	P value
Maternal age (years)					
Mean±SD	26.58±5.27	25.46±4.53	24.74±4.22	1.951	0.146
Range	18-35	18-35	18-34		
Duration of marriage(years)					
Mean±SD	5.88±4.48	5.23±4.15	4.54±3.48	2.788	0.098
Range	1-16	1-15	1-14		
Calculated gestational age(weeks)					
Mean±SD	34.58±5.14	35.104.97	35.32±4.56	0.301	0.741
Range	21-40	21-40	23-40		
Gestational age by U/S (weeks)					
Mean±SD	34.56±4.96	35.02±4.87	35.16±4.49	0.216	0.806
Range	22-40	21-40	23-40		

This table shows no statistically significant difference between groups according to patients characteristics.

Table (2): Comparison between the studied groups as regard β-HCG levels.

Level of β-HCG in vaginal fluid	Group I	Group II	Group III	t-test	P value
Mean±SD	455.80±119.27	113.24±58.38	24.75±15.15	538.363	<0.001
Range	65-732	11-290	10.3-96.4		

This table shows highly statistically significant difference between groups according to level of β HCG in vaginal fluid.

Table (3): Diagnostic performance of level of β-hCG in vaginal fluid in discrimination of studied groups.

β-HCG	Cut-off	Sen.	Spe.	PPV	NPV	AUC
Group I vs. Group II	**≥290**	96%	100%	100%	96.2%	97.4%
Group I vs. Group III	**≥62**	100%	98%	100%	98%	99.9%
Group II vs. Group III	**≥48**	98%	96%	96.1%	98%	96.9%

Table (4): Comparison between the studied groups as regard amniotic fluid index (AFI).

AFI (cm)	Group I	Group II	Group III	t-test	P value
Mean±SD	6.44±3.29	8.78±3.43	13.60±4.98	42.211	<0.001
Range	2-15	4-17	6-24		

This table shows highly statistically significant difference between groups according to AFI.

Table (5): Diagnostic performance of level of AFI (cm) in discrimination of studied groups.

AFI (cm)	Cut-off	Sen.	Spe.	PPV	NPV	AUC
Group I vs. Group II	**≤8**	80%	52%	62.5%	72.2%	69.6%
Group I vs. Group III	**≤8**	80%	80%	80%	80%	88.7%
Group II vs. Group III	**≤11**	78%	64%	68.4%	74.4%	77.9%

DISCUSSION

This study is a prospective randomized case-control study which was done to determine the role of quantitative level of β-hCG in vaginal fluid in diagnosis of premature rupture of membranes. This study was designed on pregnant women attending El-Hussien University and Sohag Teaching Hospitals in gestational age between 20 and 40 weeks. A total of 150 pregnant women were included in this study and were divided into three groups. Group I: PROM group *(n=50),* group II: suspected PROM group *(n=50)* and group III: pregnant women with no history of rupture of membranes as control group *(n = 50).*

There were no statistically significant differences in maternal age, parity, duration of marriage, gestational age at membranes rupture, presence of vaginal discharge and history of coitus within 48 hrs between patients with and without clinical evidence of membranes rupture (Table 1).

The mean vaginal fluid hCG levels in group I, group II and group III were 455.80 ± 119.27, 113.24 ± 58.38 and 24.75 ± 15.15 mIU/mL respectively at (table 2), when the difference was statistically significant (P<0.001). With hCG cut-off value ≥62 mIU/ml, the sensitivity 100%, specificity 98%, positive predictive value 100% and negative predictive value 99% with diagnostic accuracy of 99.9% in confirming PROM (table 3).

Kariman et al. (2011) (6) reported that the mean hCG level in cervicovaginal discharge of PROM group was significantly higher than the control group (330.88±436.18 vs. 6.56±5.70 mIU/mL; p=0.0001). With cut-off value of 19mIU/mL, the sensitivity was 94.5%; specificity, 91%; positive predictive value, 91.5%; negative predicted value, 94.2% and accuracy was 92.2%. Also, **Bahasadri et al. (2013) (9)** who also studied 3 groups in which, 123 pregnant women were recruited divided into 3 groups: group 1 (PROM -41 cases), group 2 (suspected PROM group, 42 cases) and group 3 (intact membranes, control group, 40 cases). HCG concentration was 468.06 ± 366.34, 176.43±316.37 and 7.71 ± 15.7mIU/mL in the 3 groups respectively with a cut-off value of 79.5mIU/mL. They concluded that hCG was higher in the cases of PROM and patients who were suspected to have PROM, and may be used as a suitable, fast and reliable test for detecting rupture of membranes. **Ghasemi et al. (2016) (10)** compared between prolactin, urea, creatinine and hCG as being effective marker in vaginal fluid for the diagnosis of PROM. A total of 160 pregnant women were recruited divided into 2 groups (PROM and control group). They reported that the mean of hCG in PROM group 203.1mIU/ml, control group 17.4 mIU/ml with cut-off value 20.5, sensitivity 87.5% and specificity 86%. **Alihan et al. (2014) (11)** also studied the role of hCG, creatinine and urea in vaginal washing fluid in the diagnosis of premature rupture of membranes. A total of 165 pregnant women were recruited divided into 2 groups (PROM & control group). They reported that the mean of hCG in PROM group 214.68 mIU/ml, control group 23.93 and P value <0.001.

The difference in the results of several studies could have arisen from reasons such as the existence of a difference in the number of samples, patient characteristics, gestational age and patients with vaginal bleeding which were included in some studies.[12]

Ultrasonogrphic AFI might be used in the diagnosis of PROM as well as having a prognostic value.

Amniotic fluid index (AFI) was lower among PROM group 6.44±3.29 compared to suspected group 8.78±3.43 and control group 13.60±4.98, with a highly statistically significant difference between both groups (table 4).

Using receiver operating characteristic (ROC) curve, it was found that ultrasonographic AFI measurements less than 8cm had 80% diagnostic sensitivity, 80% diagnostic specificity, 80%

positive predictive value (PPV) and 80% negative predictive value with diagnostic accuracy of 88.7% (table 5).

CONCLUSION

The detection of hCG in the vaginal fluid is a rapid, reliable and noninvasive method for diagnosis of premature rupture of membranes. Unlike other tests, the test is not affected by semen or vaginal discharge.

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