

**Evaluation of vaginal fluid  $\beta$ -HCG for the diagnosis of premature rupture of membranes**El-Sayed Ahmed El-Desouky<sup>1</sup>, Ashraf Elshahat<sup>1</sup>, Ahmed Abd Elhamid<sup>2</sup>, Abd Elhalim Mohammed<sup>2</sup>, Mahmoud Hashish<sup>3</sup><sup>1</sup>Department of Obstetrics & Gynecology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.<sup>1</sup>Department of Obstetrics & Gynecology, Faculty of Medicine, Al-Azhar University, Assuit, Egypt.<sup>3</sup>Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.[elsayedeldesouky@yahoo.com](mailto:elsayedeldesouky@yahoo.com)

**Abstract: Objectives:** To determine the role of quantitative level of  $\beta$ -HCG in vaginal fluid in diagnosis of premature rupture of membranes. **Design:** Case-control study. **Setting:** Department of Obstetrics and Gynecology, Al-Azhar University Hospitals. **Population:** A total of 150 consenting patients were evaluated, of whom 50 met the criteria for membranes rupture as a PROM group, 50 met suspected criteria for rupture membranes and 50 without rupture of membranes as a control group. **Methods:** quantitative level of  $\beta$ -HCG in vaginal fluid. HCG is present in AF as well as maternal blood and urine, at concentrations ranging from approximately 2000 to 70,000 mIU/mL. **Results:** It was found that HCG levels were higher among PROM group compared to suspected and control group with a highly statistically significant difference between three groups. It was observed that vaginal HCG values more than 62mIU/ml are highly predictive of membranes rupture with 100% diagnostic sensitivity, 98% diagnostic specificity, 100% PPV and 98% NPV. The performance of this marker in diagnosing PROM was therefore very good. **Conclusions:** the presence of vaginal HCG is highly predictive of membrane rupture. Although a positive result would be strongly indicative of membranes rupture, a negative result would require further confirmatory tests to completely rule out membranes rupture.

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**Key words:**  $\beta$ -HCG, PROM, vaginal fluid

## 1. Introduction

Rupture of membranes (ROM) is an important obstetrical problem, which can lead to infectious morbidity in the mother and fetus, cord accidents and imminent term or preterm labour. Preterm birth represents 75% of all the causes of perinatal morbidity and mortality (Dartibale *et al.*, 2017).

A timely and accurate diagnosis of PROM is therefore critical to optimize pregnancy outcome & to minimize serious complications (e.g., chorioamnionitis, neonatal sepsis). Conversely, a false positive diagnosis of ROM may lead to unnecessary obstetric interventions, including hospitalization, administration of antibiotics even induction of labour (Eldaly *et al.*, 2018).

Visualization of amniotic fluid pooling on speculum examination is diagnostic with 100% accuracy, but non visualization of amniotic fluid pooling does not exclude ROM (Palacio *et al.*, 2016).

Various methods are used to diagnose ROM such as nitrazine and ferning test or injection of intra-amniotic dye. The fern test & nitrazine test are not highly sensitive. Indigo carmine dye test is

considered the gold standard test for the diagnosis of PROM, yet it is an invasive procedure that carried many fetal & maternal risks (Bouzari *et al.*, 2018).

The absence of a non-invasive gold standard test for the diagnosis of PROM has led to the search for an alternative biochemical marker. The use of biochemical markers in the cervico-vaginal fluid such as alpha fetoprotein, fetal fibronectin, or insulin-like growth factor-binding protein-1 seems to present a reasonable alternative method for diagnosing ROM. All of these markers have advantages and disadvantages. However, they have not been popular because of their complexity and cost (Gezer *et al.*, 2016).

Beta Human Chorionic Gonadotropin ( $\beta$ -hCG) is a glycoprotein produced exclusively by syncytiotrophoblast in the placenta. It is present in amniotic fluid as well as maternal blood and urine, at concentrations ranging from approximately 2000-70000mIU/mL (Gezer *et al.*, 2016).

Several studies have documented the presence of low  $\beta$ -hCG level in the vaginal washings of normal pregnant women with intact membrane with

approximately nine-fold increased levels of  $\beta$ -hCG in the vaginal washings of pregnant women with PROM (Eldaly *et al.*, 2018)

Vaginal fluid human chorionic gonadotropin (hCG) is one of the biochemical markers that had been suggested for the accurate diagnosis of ROM. (Gezer *et al.*, 2016).

#### **Aim:**

The aim of our study is to evaluate the role of  $\beta$ -HCG in vaginal fluid as one of simple test for diagnosis of premature rupture of membranes.

#### **2. Patients and Methods:**

This study is a case-control study which was done to determine the role of quantitative level of  $\beta$ -HCG in vaginal fluid in diagnosis of premature rupture of membranes.

The study was carried out at Al-Azhar University hospitals. Pregnant women in gestational age between 20 and 40 weeks, attending the hospital were the subject of the study.

It was performed on 150 pregnant women divided into 3 groups as follows:

##### **Group I: (Definite rupture of membranes):**

It included 50 pregnant women with PROM with the following inclusion criteria:

1. Gestational age between 20-40 wks.
2. Singleton pregnancy.
3. History of watery vaginal leakage.
4. Visualization of amniotic fluid leakage (sterile cusco speculum examination: positive fluid leakage).
5. Decreased amniotic fluid index (AFI was calculated according to 4 quadrants technique): AFI:5-10cm.

##### **Group II: (Suspected but not Definite PROM):**

It included 50 pregnant women with suspected rupture of membranes with the following inclusion criteria:

1. Gestational age between 20-40 wks.
2. Singleton pregnancy.
3. History of watery vaginal leakage.
4. Non visualization of amniotic fluid leakage (sterile cusco speculum examination: negative fluid leakage).
5. Average amount of amniotic fluid index: AFI > 10cm.

##### **Group III: (Control Group):**

It included 50 pregnant women who were attended the outpatient clinic for routine antenatal care with the following inclusion criteria:

1. Gestational age between 20-40 wks.
2. Singleton pregnancy.

3. No history of vaginal fluid leakage.

4. Average amount of amniotic fluid index: AFI > 10cm.

##### **Inclusion criteria:**

- 1- Age from 18-35 years.
- 2- Gestational age between 20-40 wks.
- 3- Absence of regular uterine contractions.
- 4- Absences of vaginal bleeding.
- 5- Absences of vaginal infection.
- 6- No history of coitus 48 h before examination.

##### **Exclusion criteria:**

- 1- Patients at less than 20 week.
- 2- Presence of any amount of vaginal bleeding, either spontaneous or traumatic due to speculum examination.
- 3- Pregnancies complicated by oligohydramnios due to hypertension, intrauterine growth restriction (IUGR), fetal anomalies and post-term pregnancy.
- 4- Chorioamnionitis (diagnosed by: maternal fever, fetal tachycardia, leukocytosis, elevated CRP, offensive vaginal discharge).
- 5- Liver or kidney diseases.

##### **All pregnant women included in this study were subjected to:**

###### **• Full history taking:**

Including, personal history, the last menstrual period, history of amniotic fluid leakage (onset, amount, duration and color of the fluid), history of amniotic fluid leakage in previous pregnancies, past history of vaginal bleeding and obstetric history.

###### **• General examination:**

Including, vital signs ( blood pressure, pulse and temperature), pallor, jaundice, cyanosis, oedema (generalized or localized), chest and heart examination.

###### **• Abdominal examination:**

Including, fundal level, uterine contraction, fetal heart sound, abdominal tenderness and rigidity.

###### **• Transabdominal ultrasonography for:**

Gestational age, fetal viability, placental localization, congenital fetal malformation and ultrasonic assessment of amniotic fluid index using 4 quadrant technique.

###### **• Cardiotocography:**

All patients examined by CTG for half an hour and non stress tests were evaluated to exclude non reactive (positive tests).

###### **• Laboratory investigations:**

Including, total leucocytic count, CRP, liver functions and kidney functions by collecting 5ml of whole blood to be sent to the central laboratory at Al-Azhar University hospitals.

**Study Procedures:**

After taking an informed consent, history taking and general examination, all of the patients will be subjected to a speculum examination. Amniotic fluid pooling with or without vulsalva maneuver will be noted. Their history of coitus within 48 hrs of admission will be recorded. Infectious discharge and bleeding during the speculum examination will be also recorded. cervicovaginal swab will be taken from cervical canal and vaginal vault for culture and sensitivity, 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 will carried out, cervicovaginal swab will be taken for culture and sensitivity then vaginal fluid sampling will be carried out.

After confirming nitrazine test and absence of bloody discharge in the posterior fornix, the vaginal fornix will be irrigated with 3-ml of sterile saline with use of a 5-ml syringe.

With the same syringe, the vaginal washing will subsequently aspirated from the posterior fornix.

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

All of the samples will be studied in the same laboratory and by the same technique.

**Immunoassay:**

Concentrations of  $\beta$ -HCG in the sample will be measured with **IMMULITE METHOD**. This assay used an anti-HCG monoclonal antibody in the solid phase and a second monoclonal antibody conjugated to horseradish peroxidase (HRP) to amplify the HCG signal. It was designed to eliminate differential antibody recognition of various HCG phosphoforms. The assay is unaffected by the state of HCG phosphorylation, thus, permitting reliable measurement of total HCG levels. Absorbance was read at 20 mIU/mL, with a sensitivity of 0.2 mIU/mL and inter-assay and intra-assay coefficients of variation of less than 7.6% and 4.6%, respectively. The test can be performed in less than 2 hrs.

**Statistics:**

Analysis of data will be carried out to correlate between quantitative level of  $\beta$ -HCG in vaginal fluid and diagnosis of premature rupture of membranes.

Analysis of data was done by computer using Statistical Package for Science and Society (SPSS version 15) as follows:

**Description** of quantitative variables as mean (summation of values divided by their number), standard deviation (deviation of values around the mean) and range (difference between the highest and the lowest values).

**Description** of qualitative variables as frequencies (number of cases) and relative frequencies (percentages).

**Chi-square (X<sup>2</sup>):** test was used to compare qualitative variables between groups.

**One way ANOVA test (F):** a technique was used to compare means of two or more groups. This technique can be used only for numerical data.

**Unpaired t-test:** was used to compare two groups as regard quantitative variables in parametric data (SD < 25% mean).

**The Area Under ROC Curve (AUC):** was used to find out the overall productivity of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value.

**Sensitivity:** probability that a test result will be positive when the disease is present (true positive rate, expressed as a percentage).

**Specificity:** probability that a test result will be negative when the disease is not present (true negative rate, expressed as a percentage).

**Cut-off value:** the value corresponding to a given significance level. **58.**

**PPV (positive predictive value):** probability that the disease is present when the test is positive (expressed as a percentage of true positive cases to all positive).

**NPV (negative predictive value):** probability that the disease is not present when the test is negative (expressed as a percentage of true negative subjects to all negative).

**P-value (probability value):** was used to quantify the idea of statistical significance of evidence and a guideline to ignore data that didn't reach a specified significance level. It was calculated from the test value by comparing the test value with the table of the probability values.

Level of significance was set as P value < 0.05.

P value > 0.05 was considered insignificant.

P value < 0.05 was considered significant.

P value < 0.001 was considered highly significant.

**3. Results:**

The study was carried out at Al-Azhar University hospitals. Pregnant women in gestational

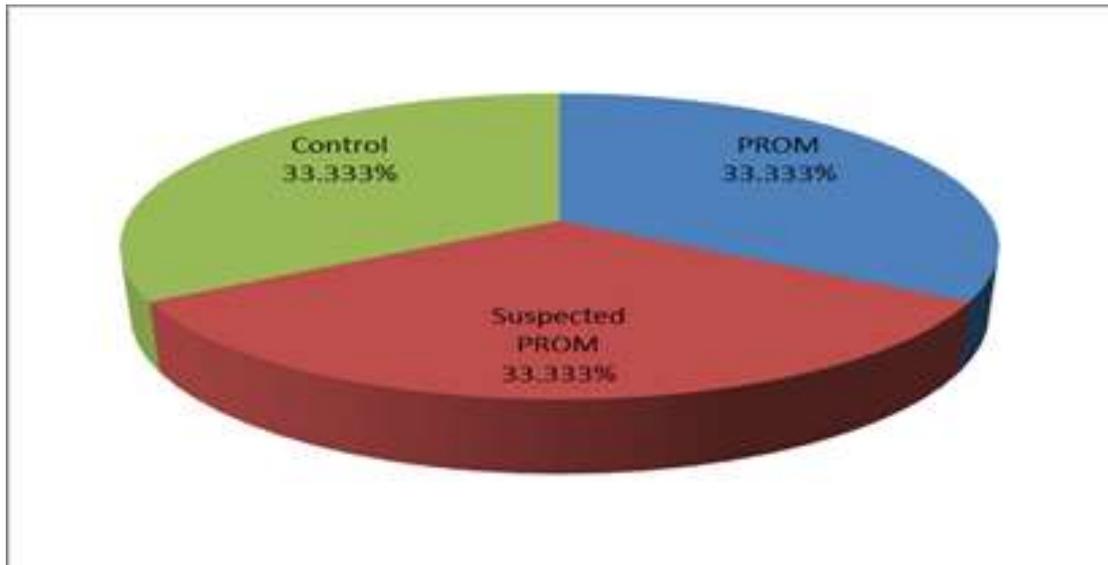
age between 20 and 40 weeks, attending the hospital were the subject of the study.

It was performed on 150 pregnant women divided into 3 groups.

**Table (1): comparison between groups according characteristics of the patients.**

	PROM GROUP	SUSPECTED PROM	CONTROL	ANOVA	P-VALUE
<b>Maternal age (years)</b>					
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		
<b>Duration of marriage (years)</b>					
Mean±sd	5.88±4.48	-	4.54±3.48	2.788	0.098
Range	1-16	-	1-14		
<b>Calculated gestational age (weeks)</b>					
Mean±sd	34.58±5.14	35.104.97	35.32±4.56	0.301	0.741
Range	21-40	21-40	23-40		
<b>Gestational age by u/s (weeks)</b>					
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 Characteristics



This Figure Shows Distribution Of The Studied Groups. A Total of 150 Patients Were Evaluated, Of Whom 50 (33.333%) As A Prom Group, 50 (33.333%) As A Suspected Prom And 50 (33.333%) As A Control Group.

**Table (2): Comparison Between The Studied Groups As Regard Vaginal Discharge.**

Vaginal discharge	Prom Group	Suspected Prom	Control	X2	P-VALUE
No	46(92.0%)	46(92.0%)	43(86.0%)	1.333	0.513
Yes	4(8.0%)	4(8.0%)	7(14.0%)		
<b>Total</b>	<b>50(100.0%)</b>	<b>50(100.0%)</b>	<b>50(100.0%)</b>		

This Table Shows No Statistically Significant Difference Between Groups According To Vaginal Discharge.

**Table (3): Comparison Between The Studied Groups As Regard History Of Coitus Within 48 Hrs.**

Coitus Within 48 Hours	Prom Group	Suspected Prom	Control	X2	P-Value
No	44(88.0%)	43(86.0%)	42(84.0%)	0.332	0.847
Yes	6(12.0%)	7(14.0%)	8(16.0%)		
Total	50(100.0%)	50(100.0%)	50(100.0%)		

This table shows no statistically significant difference between groups according to coitus within 48 hours.

**Table (4): Comparison between the Studied Groups as Regard Interval from Rupture Membranes to Sampling (Hours).**

Interval From Rupture Membranes To Sampling (Hours)	Prom Group	Suspected Prom	Control	X2	P value
Interval < 6 Hrs	22 (44%)	16 (32%)	16 (32%)	3.393	0.494
Interval Between 6-12 Hrs	18 (36%)	20 (40%)	17 (34%)		
Interval >12 Hrs	10 (20%)	14 (28%)	17 (34%)		
Mean±Sd	7.72±5.33	9.76±6.36	9.40±5.95		
Range	1-22	1-24	1-24		

This Table Shows No Statistically Significant Difference Between Groups According To Interval From Rupture Membranes To Sampling Hrs.

**Table (5): Comparison between the Studied Groups As Regard Amniotic Fluid Index (AFI).**

AFI (CM)	Prom Group	Suspected Prom	Control	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 (6): correlation between B-HCG in vaginal fluid and other parameters, using pearson correlation coefficient, of the study group.**

	Level Of B-Hcg In Vaginal Fluid					
	Prom		Suspected Prom		Control	
	R	P	R	P	R	P
Maternal Age (Years)	-0.126	0.385	-0.029	0.840	-0.119	0.412
Duration Of Marriage (Years)	-0.220	0.125	-	-	-0.131	0.364
Calculated Gestational Age (Weeks)	0.119	0.412	0.053	0.712	0.062	0.671
Gestational Age By U/S (Weeks)	0.098	0.498	0.090	0.534	0.020	0.892
Interval From Rupture Membranes To Sampling (Hours)	-0.225	0.116	-0.041	0.779	0.010	0.944
Afi (Cm)	-0.065	0.652	-0.144	0.319	0.192	0.182

**Table (7): Diagnostic Performance of Level of B-Hcg in Vaginal Fluid in Discrimination of Studied Groups.**

B-Hcg	Cut-Off	Sen.	Spe.	Ppv	Npv	Auc
PROM VS. SUSPECTED PROM	≥290	96%	100%	100%	96.2%	97.4%
PROM VS. CONTROL	≥62	100%	98%	100%	98%	99.9%
Suspected prom vs. Control	≥48	98%	96%	96.1%	98%	96.9%

Prom vs. Suspected prom: which was  $\geq 290$ , with sensitivity of 96% specificity of 100% positive predictive value of 100%, negative predictive value of 96.2% with diagnostic accuracy of 97.4.

.prom vs. Control: which was  $\geq 62$ , with sensitivity of 100% specificity of 98% positive predictive value of 100%, negative predictive value of 98% with diagnostic accuracy of 99.9%.

.prom vs. Control: which was  $\geq 62$ , with sensitivity of 100% specificity of 98% positive predictive value of 100%, negative predictive value of 98% with diagnostic accuracy of 99.9%.

•suspected prom vs. Control: which was  $\geq 48$ , with sensitivity of 98% specificity of 96% positive predictive value of 96.1%, negative predictive value of 98% with diagnostic accuracy of 96.9%.

**Table (8): diagnostic performance of level of afi (cm) in discrimination of studied groups.**

AFI (CM)	CUT-OFF	SEN.	SPE.	PPV	NPV	AUC
Prom Vs. Suspected Prom	$\leq 8$	80%	52%	62.5%	72.2%	69.6%
Prom Vs. Control	$\leq 8$	80%	80%	80%	80%	88.7%
Suspected Prom Vs. Control	$\leq 11$	78%	64%	68.4%	74.4%	77.9%

#### Receiver operating characteristics (roc) curve was used to define the best cut off value of afi:

- Prom vs. Suspected prom: which was  $\leq 8$ , with sensitivity of 80% specificity of 52% positive predictive value of 62.5%, negative predictive value of 72.2% with diagnostic accuracy of 69.6%.

- Prom vs. Control: which was  $\leq 8$ , with sensitivity of 80% specificity of 80% positive predictive value of 80%, negative predictive value of 80% with diagnostic accuracy of 88.7%.

- Suspected prom vs. Control: which was  $\leq 11$ , with sensitivity of 78% specificity of 64% positive predictive value of 68.4%, negative predictive value of 74.4% with diagnostic accuracy of 77.9%.

#### 4. Discussion:

This study is a case-control study which was done to determine the role of quantitative level of  $\beta$ -HCG in vaginal fluid in diagnosis of premature rupture of membranes. This study was designed on pregnant women attending Alzhar university hospitals in gestational age between 20 and 40 weeks. A total of 150 pregnant women were included in the study and were divided into three groups. Group I: ROM group (n=50), Group II: suspected ROM 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.

Quantitative assay of hCG for diagnosis of ROM was more reliable than usual methods such as fern or nitrazine tests and even speculum examination as measurement of hCG are not affected by interfering factors like fern or nitrazine test. On the other hand, when speculum examination

is performed with a delay after rupture of membranes, it may not be helpful, while, high concentration of hCG can be detectable in cervicovaginal secretions after rupture of membranes (Magann et al., 2017)

In the current study,: The mean vaginal fluid hCG levels in Group (I), Group (II) and Group (III) were  $455.80 \pm 119.27$ ,  $113.24 \pm 58.38$  and  $24.75 \pm 15.15$  mIU/mL respectively, The difference was statistically significant ( $P < 0.001$ ). With hCG cut-off value  $\geq 62$  mIU/ml, the sensitivity 100%, specificity 98%, positive predictive value 100%, negative predictive value 99% with diagnostic accuracy of 99.9% in confirming ROM. Kariman et al., (2017) studied only two groups and reported that the median and range of vaginal fluid  $\beta$ -HCG were 6.3 (0.6-62.2) mIU/ml in pregnant women without ROM and 420.6 (216-918.3) mIU/ml in pregnant women with ROM. They considered vaginal  $\beta$ -HCG cut-off value of  $\geq 50$  mIU/ml as an accurate diagnostic tool of ROM.

Kacerovsky et al., (2016), did the same & the mean  $\beta$ hCG levels were  $250.60 \pm 118.6$  mIU/ml in ROM group and  $6.2 \pm 10.6$  mIU/ml in intact membrane group with cut-off value of 22.32 mIU/ml.

Later on, Kariman N et al., (2017) reported that the mean HCG level in cervicovaginal discharge of ROM group was significantly higher than the control group ( $330.88 \pm 436.18$  vs.  $6.56 \pm 5.70$  mIU/mL;  $p = 0.0001$ ). With cut-off value of 19 mIU/mL, the sensitivity was 94.5%; specificity, 91%; positive predictive value, 91.5%; negative predicted value, 94.2% and accuracy was 92.2.

Magann et al., (2017) analyzed data from 52 normal pregnant women, divided into three groups: 20 pregnant women without ROM, 21 patients with confirmed ROM, 11 patients with suspected ROM

using hCG cut-off value of 100 mIU/ml. They found that there is no overlapping between the hCG levels of the group of pregnant women without ROM and the group of patients with confirmed ROM. They concluded that hCG levels in the washing fluid of the posterior vaginal fornix is a useful, very cheap and non-invasive diagnostic test of ROM. **Eldaly et al., 2018** also studied 3 groups. 141 pregnant women were recruited divided into 3 groups: group 1 (confirmed ROM - 34 patients), group 2 (suspected but unconfirmed ROM - 39 patients) & group 3 (control group - 68 pregnant women without any complaint or complication). Geometric mean values of hCG were found to be 95, 14 & 10 mIU/ml for the 3 groups respectively & the optimal cut-off was a hCG value of 65 mIU/ml. They concluded that vaginal washing fluid hCG is reliable, simple and rapid test for the diagnosis of ROM.

Similarly, **Bahasadri et al., (2018)** who also studied 3 groups. 123 pregnant women were recruited divided into 3 groups: group 1 (ROM -41 cases), group 2 (suspected ROM group- 42 cases) & group 3 (intact membranes - control group - 40 cases).

HCG concentration was  $468.06 \pm 366.34$ ,  $176.43 \pm 316.37$  &  $7.71 \pm 15.7$  mIU/mL in the 3 groups respectively with a cut-off value of 79.5 mIU/mL. They concluded that hCG was higher in the cases of ROM and patients who were suspected to have ROM, and may be used as a suitable, fast and reliable test for detecting rupture of membranes.

**Beckmann et al., (2016)** compared between prolactin, alphafetoprotein (AFP) & HCG as being effective marker in vaginal fluid for diagnosing ROM. A total of 100 pregnant women were recruited divided into 2 groups (ROM & control group). Vaginal fluid concentrations of the three markers were significantly higher in the ROM group than in the control (intact) group ( $p < 0.001$ ). They also reported that AFP had the highest diagnostic performance as AFP had 94% specificity, sensitivity, positive and negative predictive values, and efficiency but the other two markers had lower specificity, sensitivity, positive and negative predictive values, and efficiency (70, 76, 71.7, 74.5 and 73% for prolactin and 72, 84, 75, 81.8 and 78% for BhCG, respectively).

**Cunningham et al., (2014)** also compared between vaginal fluid prolactin & hCG as diagnostic markers for ROM. Total of 211 women were included divided in 2 groups. Prolactin levels in ROM group were  $2930 \pm 3737$  mIU/l versus  $23.18 \pm 120$  mIU/l in the control group ( $P=0.000$ ). hCG was  $439.78 \pm 1867$  mIU/l in ROM and  $17.72 \pm 30$  mIU/l in control group ( $p=0.000$ ). Sensitivity and specificity of prolactin according to

cutoff of 16 mIU/l was 79.41% and 96%, respectively. Sensitivity and specificity for hCG with cut-off point of 12.5 was 69.85% and 69.33%, respectively. They concluded that measurement of prolactin and hCG levels in patients with suspected rupture of membranes can help in decision-making and treatment.

**Ghasemi et al., (2016)** compared between prolactin, urea, creatinine & HCG as being effective marker in vaginal fluid for diagnosing ROM. A total of 160 pregnant women were recruited divided into 2 groups (ROM & control group). They reported that the mean of HCG in ROM group 203.1 mIU/ml, control group 17.4 mIU/ml cut of value 20.5 sensitivity 87.5% specificity 86%. (**Alihan Tigli et al., 2016**) 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 (ROM & control group). They reported that the mean of HCG in ROM group 214.68 mIU/ml, control group 23.93 and P value  $< 0.001$ .

The different in results in the several studies could have arisen from reasons such as the existence of a difference in the number of samples, patient characteristics, gestational age & patients with vaginal bleeding were included in some studies (**Espinoza et al., 2016**)

The study showed that no statistically significant difference detected between the studied groups as regard maternal age,  $26.58 \pm 5.27$ ,  $25.46 \pm 4.53$  and  $24.74 \pm 4.22$ , respectively or gestational age,  $34.56 \pm 4.96$ ,  $35.02 \pm 4.87$  and  $35.16 \pm 4.49$  respectively ( $p\text{-value} > 0.806$ ).

These results are consistent with the study performed by **Masho et al., 2017** who reported mean gestational age in confirmed PROM group and control group,  $32.9 \pm 1.6$  and  $33.1 \pm 1.9$  respectively with no statistically significant differences between the studied groups.

Also, these results are consistent with the study performed by **Mercer et al., 2016**, who found that there were no statistically significant differences between confirmed PROM group and unconfirmed PROM group as regard maternal age and gestational age, at time of obtaining the sample.

Also, these results are consistent with the study performed by **Anai et al., 2017**, who found that there were no statistically significant differences between confirmed PROM group and unconfirmed PROM group as regard parity.

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

Amniotic fluid index (AFI) was lower among PROM group  $6.44 \pm 3.29$  compared to suspected

group  $8.78 \pm 3.43$  and control group  $13.60 \pm 4.98$ , with a highly statistically significant difference between both groups. (Table 5)- (Figure 19)

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 9)- (Figure 24).

**Mercer et al et al., (2016)** reported that Low AFI (<5cm) and low maximum vertical fluid pocket (MVP < 2cm) had identified 67.2% and 46.9% of women with ROM, respectively.

**Cole et al., (2017)** reported that a reduction in the four quadrant AFI below 80 mm did not reliably identify cases of suspected membrane rupture by history with negative visualization of fluid by speculum examination. They also compared between nitrazine test and AFI in the diagnosing of ROM in suspected cases. The sensitivity, specificity and accuracy of the nitrazine test, the PROM test and AFI were 97, 16 and 56%, versus 94, 91 and 92%, respectively. They also reported that the measurement of AFI offers no advantage over measurement of a single vertical pocket of fluid in cases where ultrasound is used to evaluate possible membrane rupture.

### Conclusions:

The detection of HCG in the vaginal fluid is a rapid, reliable and noninvasive method for diagnosis of premature rupture of membranes.

### Recommendations

Estimation of quantitative vaginal beta HCG is gold standard test for diagnosis of PROM and it is most faster Reliable and non invasive test for diagnosis of PROM. It should be used in the cases suspected PROM.

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