

# **Measurement of Vaginal Fluid Urea and Creatinine as a Simple Test to Confirm Diagnosis of Premature Rupture of Membranes**

## **Thesis**

Submitted for partial fulfillment of the master degree  
In Obstetrics and Gynecology

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## **List of Abbreviations**

<b>AF</b>	: Amniotic Fluid
<b>AFI</b>	: Amniotic Fluid index
<b>AFP</b>	: Alpha fetoprotein
<b>AFV</b>	: Amniotic Fluid Volume
<b>ANOVA</b>	: Analysis of Variance
<b>AUC</b>	: Area under the curve
<b>BPP</b>	: Biophysical Profile
<b>BV</b>	: Bacterial Vaginosis
<b>CIN</b>	: Cervical Intraepithelial Neoplasia
<b>DAO</b>	: Diamine Oxidase
<b>ECells</b>	: Epithelial-like cells
<b>FCells</b>	: Fibroblast-like cells
<b>fFN</b>	: Fetal Fibronectin
<b>FHR</b>	: Fetal Heart Rate
<b>HCG</b>	: Human Chorionic Gonadotropin
<b>IGF</b>	: Insulin Growth Factor
<b>IGFBP-1</b>	: Insulin Growth Factor Binding Protein-1
<b>LEEP</b>	: Loop Electrosurgical Excision Procedure
<b>LLETZ</b>	: Large Loop Excision of the Transformation Zone
<b>LMP</b>	: Last Menstrual Period
<b>MMP</b>	: Matrix Metalloproteinase
<b>MVP</b>	: Maximal Vertical Pocket
<b>NPV</b>	: Negative Predictive Value
<b>PBEF</b>	: Pre-B-cell Colony Enhancing Factor
<b>PPROM</b>	: Preterm Premature Rapture of Membranes
<b>PPV</b>	: Positive Predictive Value
<b>PROM</b>	: Premature Rapture of Membranes
<b>ROC</b>	: Receiver Operating Characteristic
<b>ROM</b>	: Rapture of Membranes
<b>ROS</b>	: Reactive Oxygen Species
<b>SD</b>	: Standard Deviation
<b>SPSS</b>	: Statistical Package for Social Sciences
<b>2-DP</b>	: Two-diameter poc

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**MEASUREMENT OF VAGINAL FLUID UREA  
AND CREATININE AS A SIMPLE TEST TO  
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**Protocol of thesis**

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# Introduction

Premature rupture of membranes (PROM) is the rupture of the fetal membranes before the onset of labor, It occurs in 10% of all gestation (*Modena et al., 2004*).

Correct diagnosis of PROM has a great importance because failure of diagnosis can lead to unwanted obstetric complications like fetal and maternal infection, cord complication and chorioamnionitis. On the other hand, over diagnosis can lead to unnecessary interventions like hospitalization, administration of antibiotics and corticosteroids (*Wiberg-Itzel et al., 2005*).

Methods of diagnosis of PROM include history, physical examination and selected laboratory studies. Patients often report a sudden gush of fluid with continued leakage, the physician performs a speculum examination to evaluate evidence of fluid pooling in the vagina or leaking from the cervical os when the patient coughs, presence of a nitrazine/ferning positive, but the nitrazine and ferning tests can be falsely positive (*Kim et al., 2005b*).

Laboratory tests include the measurement of vaginal PH, prolactin, Alpha Fetoprotein (AFP), Diamine Oxidase (DAO), Insulin like Growth Factor binding Protein-1 (IGFBP-1),

human chorionic gonadotropin and Fetal Fibronectin. All these tests have advantages and drawbacks, up to now there is no gold standard diagnostic test for PROM (*Esim E et al., 2003*).

As the Fetal urine is the most important source of amniotic fluid in the second half of pregnancy. So, vaginal fluid urea and creatinine may be helpful in diagnosis of PROM (*Kafali and Oksuzler, 2007*).

Vaginal fluid creatinine determination has been used in the clinical studies to diagnose PROM (*Li and Chang, 2000; Gurbuz et al., 2004*).

A previous study by (*Kafali H and Oksuzler C, 2007*) showed that vaginal washing fluid urea and creatinine use for the diagnosis of PPRM is reliable, simple and rapid test with sensitivity and specificity of 90-100%.

## **Aim of the Study**

The aim of the study is to test the use of vaginal fluid creatinine and urea as a simple test to confirm the diagnosis of premature rupture of membranes.

### **Research question**

Does measuring vaginal fluid urea and creatinine can be used as a simple test to confirm the diagnosis of premature rupture of membranes?

### **Research hypothesis:**

As the urine is the main source of amniotic fluid, so urea and creatinine are increased in amniotic fluid; therefore, vaginal urea and creatinine of a pregnant woman can be used as a simple test to confirm premature rupture of membranes.

## **Patients and Methods**

The study will include 96 pregnant women between 28-40 weeks of pregnancy attending Ain Shams Maternity University hospital.

The 96 pregnant women will be classified into three groups:

### **Group 1:**

Includes 32 pregnant women complaining of leakage of watery vaginal fluid which confirmed by speculum examination which show fluid pooling in the vagina or leaking from the cervical os when the patient cough and amniotic fluid index (AFI) measurement below 8 cm.

### **Group 2:**

Includes 32 pregnant women complaining of leakage of watery vaginal fluid which was not demonstrated by fluid pooling in the vagina or leaking from the cervical os under speculum examination and/or amniotic fluid index (AFI) measurement.

### **Group3:**

Includes 32 normal pregnant women with no complains as a control group.

All groups will be subjected to the following:

- Full history.
- General examination.
- Underwent speculum examination for confirmation of premature of membranes and for Urea and creatinine sampling.(speculum examination will be negative if no fluid pooling in the vagina or leaking from the cervical os when the patient cough).

Ultrasonographic examination for gestational age determination and amniotic fluid index which will be done at ultrasonographic unit in Ain Shams Maternity University Hospital using multiple pockets method by sum total of the deepest vertical pockets in each of the four quadrants into which the uterus is divided by using the umbilicus and the linea nigra as reference point for the upper and lower halves and for the left and right halves, respectively.

**Inclusion criteria:**

- Gestational age between 28-40 weeks.
- Pregnant women that report a leakage of vaginal watery fluid.

**Exclusion Criteria:**

- Maternal kidney impairment.
- Fetal renal malformation.
- Vaginal bleeding.
- Vaginal infection.
- Polyhydramnios.

After taking full history, complete clinical examination, pelvic ultrasound.

Collection of vaginal sample will be done as following:

- The pregnant woman will lie in the lithotomy position.
- Sterile speculum examination will be done.
- 5 ml of sterile saline will be injected into the posterior fornix using sterial syringe.
- 3ml of the injected saline will be aspirated using the same syringe.
- This sample will be sent to the laboratory to be tested for the level of creatinine and urea.

## **Statistical analysis**

### **Sample Size Justification**

Sample size was calculated using EpiInfo® version 6.0, setting the type-1 error ( $\alpha$ ) at 0.05 and the power ( $1-\beta$ ) at 0.8. Data from a previous study (Kafali and Oksüzler 2007) showed that the mean vaginal fluid urea concentration was  $34.6 \pm 5.3$  mg/dl (in women with PPRM) and  $1.3 \pm 6.2$  mg/dl (in control group) [ $p < 0.001$ ], and that the mean vaginal fluid creatinine concentration was  $1.5.6 \pm 0.3$  mg/dl (in women with PPRM) and  $0.28 \pm 0.23$  mg/dl (in control group) [ $p < 0.001$ ]. Calculation according to these values produced a sample size of 29 cases in each group. Assuming a drop-out rate of 10% (loss of contact during follow-up), a minimum of 32 cases should be, therefore, included in each group.

Data will be collected, tabulated, analyzed by a computer software SPSS.

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