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

By

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Ayat Ezzat Mandouh Shouman

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List of Abbreviations

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

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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 PPROM 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 complainas 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 (α) at 0.05 and the power (1-β) at 0.8. Data from a previous study (Kafali and Oksüzler 2007) showed that the mean vaginal fluid urea concentration was 34.6 ± 5.3 mg/dl (in women with PPROM) and 1.3 ± 6.2 mg/dl (in control group) [$p<0.001$], and that the mean vaginal fluid creatinine concentration was 1.5.6 ± 0.3 mg/dl (in women with PPROM) and 0.28 ± 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.

References

Esim E, Turan C, Unal O, Dansuk R and Cengizglu B (2003): Diagnosis of premature rupture of membranes by identification of beta-HCG in vaginal washing fluid. Eur J Obstet Gynecol Reprod Biol.

Gurduz A; Karateke A; Kbaca C (2004): Vaginal fluid creatinine in premature rupture of membranes. Int J Gynecol Obstet.

Kafali H and Oksuzler C (2007): Vaginal fluid urea and creatinine in diagnosis of premature rupture of membranes. Arch Gynecol Obestet.

Kim YH, Park YW, Kwon HS, Kwon JY and Kim BJ (2005b): Vaginal fluid beta-human chorionic gonadotropin level, in the diagnosis of premature rupture of membranes. Acta Obstet Gynecol Scand; 84: 802-805.

Li HY and Chang TS (2000): Vaginal fluid creatinine, human chorionic gonadotropin and alpha-fetoprotein levels for detecting premature rupture of membranes. Zhonghua Yi Xue Za Zhi (Taipei).

Modena AB, Kaihura C and Fieni S (2004): Prelabour rupture of the membranes: recent evidence. Acta Bimed Atreneo Parmense.

Wiberg-Itzel E, Cnattingias S and Nordstrom L (2005): Lactate determination in vaginal fluids: a new method in the diagnosis of prelabour rupture of membranes. BJOG; 112: 754-758.