

Assessment of Urea and Creatinine in Vaginal Washing Fluid as a Method for Diagnosis of Premature Rupture of Membranes

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Abstract

Background: Premature rupture of membranes (PROM) refers to rupture of fetal membranes prior the onset of labor. If it occurs before 37 weeks of pregnancy, it is known as preterm premature rupture of membrane (PPROM). Prolonged duration from PROM till delivery is associated with increased maternal and neonatal morbidities, in term and preterm pregnancies. This includes chorioamnionitis, fetal and neonatal sepsis, placental abruption, prematurity, umbilical cord prolapse, and increased rate of cesarean delivery.

Pregnant women with history of vaginal leaking or ultrasound evidence of diminished amniotic fluid should be carefully evaluated to avoid adverse pregnancy outcomes. Accurate diagnosis helps obstetricians to optimize maternal and neonatal outcomes by early intervention to decrease morbidities.

Diagnosis of PROM is may be easy by inspection of leaking through the cervix or fluid accumulation via speculum examination. However, with small rupture of membrane or rupture bag of hind-water, it is difficult to see amniotic fluid leakage clearly and diagnosis can't be easily made, which might lead to delay in diagnosis and management.

Methods of PPROM diagnosis include fern and nitrazine which are two commonly used and traditional tests. They are rapid and easy tests but not completely reliable because of high false positive and negative results, which may be related to technical errors or contamination by blood, semen or cervical mucus.

Ultrasound evaluation of amniotic fluid can't differentiate PROM from other causes of oligohydramnios. However, tampon or amnio-dye test is a test of accurate diagnosis through aspiration and dye injection into amniotic fluid under ultrasound guidance. It is an aggressive test with has a risk of bleeding, placental abruption infection, miscarriage, and iatrogenic uterine perforation.

The Amnisure test for ROM is accurate but expensive and not available in many centers. Thus, a simple, non-invasive, and inexpensive method of detecting PROM is needed. Urea and creatinine are excreted by kidneys through glomerular filtration. Amniotic fluid also contains these markers and their determination in the vaginal can be used as a diagnostic test for PROM.

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Aim of Study: This study was conducted to evaluate the diagnostic value of urea and creatinine levels in vaginal wash in patients with suspected PROM.

Patients and Method: The study was carried out at Obstetrics and Gynecology Department, Zagazig University Hospitals. A total of 228 pregnant women were included in study, between completed 24 weeks to completed 37 weeks' gestation. Divided into two equal groups: Group A with definite PROM, control Group is B. All pregnant women included in this study were subjected to: Full history taking, general, abdominal and speculum examination, fern test and nitrazine test. Vaginal wash urea measurement by enzymatic urease examination method and vaginal wash creatinine measurement by RATE JAFFE method.

Results: The study showed that there is statistically significant difference between the two groups regarding vaginal wash urea and creatinine. The best cut-off value of vaginal wash urea in prediction of PROM is ≥ 6.85 mg/dl with AUC of 0.958, sensitivity of 98.2%, specificity of 70.2%, PPV of 76.7%, NPV of 97.6% and accuracy of 93%. The best cut-off value of vaginal wash creatinine in prediction of PROM is ≥ 0.465 mg/dl with AUC of 0.992, sensitivity of 100%, specificity of 80.7%, PPV of 83.8%, NPV of 100% and accuracy of 90.4%. Combined use of vaginal wash urea and creatinine in prediction of PROM had sensitivity of 98.3%, specificity of 91.2%, PPV of 91.8%, NPV of 98.1% and accuracy of 94.7%.

Conclusion: This study concluded that urea and creatinine assay in vaginal fluid is cheaper, faster and more valid test, possible candidate for being a gold standard test for diagnosis of PROM.

Key Words: Urea – Creatinine – Premature Rupture of Membranes (PROM).

Introduction

PREMATURE rupture of membrane (PROM) is a break in the amniotic sac prior the onset of labor after 37 weeks' gestation. Pregnant women usually claim a gush or a steady fluid leaking per vagina. If it's developed before 37 weeks' gestation, it is called PPROM (preterm premature rupture of membrane) [1]. PROM diagnosis is difficult with slow leaking, associated vaginal bleeding, or if there is no history of gush of fluid.

Risk factors include infection of the amniotic fluid, weak membranes, antepartum hemorrhage, genetic, smoking, and underweight mothers. Fetal complications may include prematurity, cord compression or infection. Maternal complications may include chorioamnionitis, placental abruption or postpartum endometritis [2].

Ultrasound evaluation of amniotic fluid can't differentiate PROM from other oligohydramnios causes. The Amnisure test is a new test for detection of PROM. It's minimally invasive, fast, and easy with high specificity and sensitivity. However, Amnisure it is expensive and not available in many centers [3].

Hence, a simple, inexpensive, and non-invasive method of detecting PROM is needed. Several markers have been studied such as fetal fibronectin, α -fetoprotein, insulin growth factor binding protein 1, urea, creatinine, β -hCG, and prolactin. Urea and creatinine are excreted by the kidneys through glomerular filtration, and also available within the amniotic fluid and have been used for PROM testing [4].

Kariman et al. [5] studied vaginal wash fluid for urea and creatinine levels. 84 pregnant women in two equal groups, one with confirmed PROM and the other include controls. The mean level of urea and creatinine in vaginal fluid in the PROM group was significantly higher than in intact fetal membranes group. They considered that measuring urea and creatinine of cervico-vaginal wash fluid confirms PROM diagnosis in the absence of blood and urine contamination.

Patients and Methods

This cross-sectional study was carried out at the Department of Obstetrics and Gynecology, Zagazig University Hospitals in the period from April 2018 to April 2019. It was based on clinical and biochemical parameters. It included 228 pregnant with gestational age from completed 24 weeks' gestation onwards.

Ethical Committee of Zagazig University Hospitals approved the study and informed written consent was taken from all patients.

Patients were divided into 2 equal groups as follows:

Group A (definite ROM):

It comprised 114 pregnant women with PROM with the following inclusion criteria:

- 1- Gestational age from completed 24 weeks to completed 37 weeks.

- 2- Singleton pregnancy.
- 3- History of watery vaginal discharge.
- 4- Positive fluid leaking by sterile Cusco speculum examination.

Group B (control group):

It comprised 114 pregnant women who were attending the outpatient clinic for routine antenatal care with the following inclusion criteria:

- 1- Gestational age from completed 24 weeks to completed 37 weeks.
- 2- Singleton pregnancy.
- 3- No history of vaginal fluid leaking.
- 4- Average amount of liquor.

Exclusion criteria:

- Blood seen in the vaginal secretion.
- Meconium stained liquor.
- History of coitus in the previous night.
- Using vaginal drugs.
- Sonographic evidence of IUFD or fetal malformation.
- Patients in labor.

Methods: All recruited pregnant women were subjected to:

Full history taking:

Personal history, LMP, history of fluid leaking (amount, onset, duration and fluid color), obstetric history and past history of fluid leaking or vaginal bleeding in previous pregnancies.

General examination:

Vital signs (pulse, temperature, blood pressure and respiratory rate), jaundice, pallor, cyanosis, edema (generalized or localized), heart and chest examination.

Abdominal examination:

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

Results of speculum examination, fern test and nitrazine test:

- 1- Pooling test: Inspection of amniotic fluid pooling in the vagina.
- 2- Nitrazine test: Nitrazine is a pH indicator dye often used in medicine. Fluid collected from the vagina by a sterile cotton swab is placed on nitrazine paper. Normal vaginal secretions are acidic (pH 4.5-6), while amniotic fluid is alkaline (pH 7.1-7.3) and will turn the nitrazine paper from orange to blue. A blue strip means it's most likely the membranes have ruptured.

3- Ferning test: Fluid collected from the vagina by a sterile cotton swab is placed on a slide and examined by microscope. Amniotic fluid is left to dry and seen under a microscope, it will form crystals resembling fern plant leaves called arborization.

Patients with confirmed pooling, positive nitrazine paper test and positive fern test were categorized as (Group A). On the other hand, patients with negative results for these tests were taken as (Group B).

Transabdominal ultrasonography:

For assessment of fetal viability, Gestational age, placental site, fetal anomalies and amniotic fluid index. Gestational age was determined based on reliable first day of LMP, or one ultrasound in before 24 weeks or two ultrasound documents between 24 and 37-weeks' gestation.

Vaginal wash urea measurement by enzymatic urease method:

Urea Agar is used for the differentiation of enteric bacilli. The urease test is used to determine the organism ability to split urea, through the production of urease enzyme.

Interpretation of urease test:

Positive Reaction: Change to bright pink color, usually complete after 3-5 hours at 35 °C.

Negative Reaction: No color change.

Vaginal wash creatinine measurement test by Jaffe reaction:

The Jaffe reaction is a colorimetric test used to determine the level of creatinine in urine and blood. Creatinine from the sample combines with the reagent to quantitatively produce an orange color with picric acid in alkaline medium. Color is developed after incubation at room temperature for 15min and measured at 520nm. The change in color is directly prorated with creatinine concentration. The Jaffe reaction, in spite of being old nonspecific test for creatinine, but still greatly appointed as the method of choice for creatinine testing because of its speed, flexibility in automated analysis, and cost-effectivity.

Statistical analysis:

Data were processed, verified and analyzed using Epi-info version 6 and SPP for Windows (6). Data were summed up using mean, Standard Deviation (SD) Sensitivity, Specificity, Accuracy and Predictive values.

The magnitude of significance is belayed at 5% level (p -value).

The outcome is deemed:

- Significant when the error prospect is <5% ($p < 0.05$).
- Non-significant when the error prospect is >5% ($p > 0.05$).
- Highly significant when the error prospect is <0.1 % ($p < 0.001$).
- Higher significance is related to smaller p -values.

Results

This cross-sectional study was executed at the Obstetrics and Gynecology Department, Zagazig University Hospitals in the period from April 2018 to April 2019. It was based on clinical and biochemical parameters. It was performed on 228 pregnant women with gestational age from completed 24 weeks onwards They divided into: Group A (definite rupture of membranes) included 114 pregnant women with history of ROM and Group B (control group) included 114 pregnant women attending the outpatient clinic for routine antenatal care.

Table (1) found no significant difference between both groups regarding age and BMI. In Table (2) also, no statistically significant difference between both groups regarding onset of leakage, gestational age, gravidity, parity or history of miscarriage.

On other side, Table (3) showed there is a statistically significant difference between both groups regarding AFI, but there are no statistically significant differences between systolic, diastolic blood pressure, respiratory and heart rates and temperature among the studied groups.

There is a statistically significant difference between the two groups regarding vaginal wash urea and creatinine as Table (4) showed.

Table (5) showed the best cutoff of vaginal wash urea in prediction of PROM is ≥ 6.85 mg/dl with AUC 0.958, sensitivity 98.2%, specificity 70.2, PPV 76.7, NPV 97.6% and accuracy 93% ($p < 0.05$).

On other hand the best cutoff vaginal wash creatinine in prediction of PROM is ≥ 0.465 mg/dl with AUC 0.992, sensitivity 100, specificity 80.7, PPV 83.8, NPV 100, and accuracy 90.4% ($p < 0.05$). Table (6) demonstrated that performance of combined vaginal wash urea and creatinine in both

groups in prediction of PROM had a sensitivity of 98.3%, specificity 91.2%, PPV 91.8%, NPV 98.1% and accuracy 94.7%.

Table (1): Comparison of age and BMI among studied groups.

	PROM	Control	<i>t</i>	<i>p</i>
Age:				
Mean ± SD	27.44±6.97	28.65±7.69	-0.881	0.380
BMI:				
Mean ± SD	24.53±5.56	25.67±6.12	-1.041	0.3

Table (2): Comparison of obstetric data among studied groups.

	PROM	Control	MW	<i>p</i>
Gestational age (weeks):				
Range	24-36	24-34	<i>t</i>	0.540
Mean ± SD	31.6±3.67	31.19±3.34	(0.614)	
Gravidity:				
Range	1-6	1-7	-0.754	0.451
Mean ± SD	3.04±1.8	3.33±1.8		
Parity:				
Range	0-5	0-5	-0.860	0.390
Mean ± SD	1.82±1.85	2.12±1.77		
Abortion:				
Range	0-3	0-3	-0.643	0.520
Mean ± SD	0.47±1.1	0.46±0.95		
Onset of leakage (days):				
Range	0.04-7	0.04-7	-1.044	0.296
Mean ± SD	1.14±1.55	1.67±1.96		
	N (%)	N (%)	X ²	<i>p</i>
History of PROM:				
Negative	15 (26.3) %	47 (82.5) %	36.21	<0.001 **
Positive	42 (73.7) %	10 (17.5) %		

t independent sample *t*-test
 MW Mann-Whitney test
p≤0.05 is significant.

Table (3): Comparison of amniotic fluid index and vital signs values among studied groups.

	PROM	Control	<i>t</i>	<i>p</i>
	Mean ± SD	Mean ± SD		
Systolic blood pressure	103.86± 9.78	104.47± 9.94	-0.333	0.740
Diastolic blood pressure	69.56±5.85	70.7±5.86	-1.04	0.3
Respiratory rate	15.39±1.4	15.44±1.4	-0.2	0.842
Heart rate	73.04±3.79	72.98±3.78	0.074	0.941
Temperature	37.4±0.32	37.4±0.32	0.087	0.930
AFI	7.02±1.64	13.39±2.34	-19.512	0.380

AFI: Amniotic fluid index.

Table (4): Comparison of urea and creatinine levels (ml/dl) in vaginal wash fluid among studied groups.

	PROM	Control	<i>t</i>	<i>p</i>
	Mean ± SD	Mean ± SD		
Urea	13.45±3.48	6.52±1.89	13.219	<0.001 **
Creatinine	1.78±0.55	0.36±0.13	MW (-9.099)	<0.001 **

t independent sample *t*-test.
 MW Mann-Whitney test.
p≤0.001 is highly significant.

Table (5): The accuracy of urea and creatinine in vaginal wash fluid in PROM prediction among studied cases.

	Cutoff	AUC	Sensi- tivity	Speci- ficity	PPV	NPV	Accuracy
Urea	6.85 mg/dl	0.958	98.2	70.2	76.7	97.6	93
Creatinine	0.465 mg/dl	0.994	100	80.7	83.8	100	90.4

Table (6): Performance of combined vaginal wash urea and creatinine in prediction of PROM among study cases.

	PROM	Control	Total
Screening test positive	102	10	112
Screening test negative	12	104	116
Total	114	114	228

	Value
Sensitivity	98.3
Specificity	91.2
PPV	91.8
NPV	98.1
Accuracy	94.7

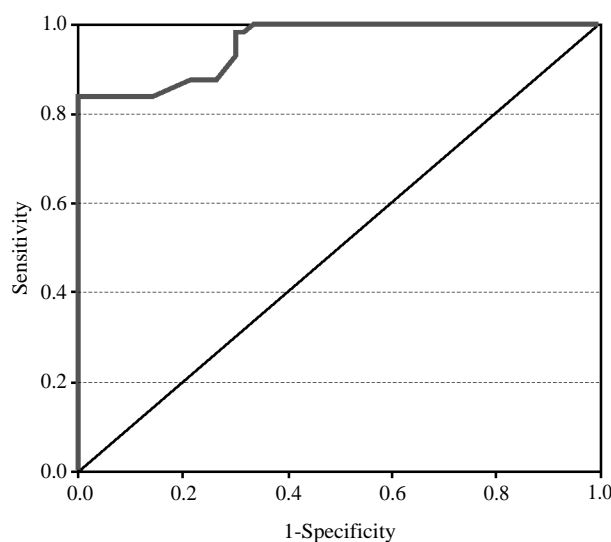


Fig. (1): ROC curve showing performance of vaginal wash urea in prediction of PROM in studied patients.

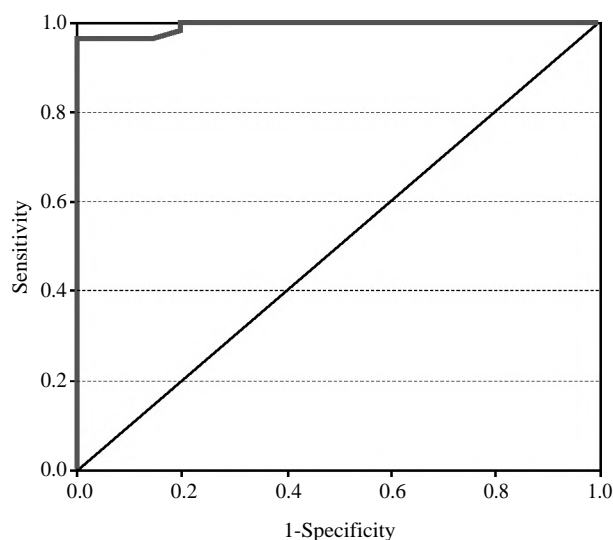


Fig. (2): ROC curve showing performance of vaginal wash creatinine in prediction of PROM in studied patients.

Discussion

PROM refers to rupture of fetal membrane before the onset of labor. PROM occurs in about 8% of term pregnancies and about 30% of preterm pregnancies, with risk of infection and preterm birth [7].

The falsely diagnosed rupture of membranes may lead to improper management such as hospital admission or induction of labor. Therefore, establishment of a crucial diagnosing of rupture of membranes is strongly needed in doubtful cases without deferral [8].

PROM is diagnosed clinically and it is suspected by a typical history of vaginal discharge watery in nature and is confirmed on sterile speculum examination. The conventional gold standard minimally invasive tests for PROM diagnosis based on: inspection of fluid leaking from the cervical os or clear fluid pooling into the posterior vaginal fornix by sterile speculum examination and microscopic ferning or changed color of nitrazine paper to blue denoting alkalinity of the cervico-vaginal discharge [9].

Diagnose of PROM by history has been shown to be reliable only in 10-50% of patients. However fluid leaking inspection from cervix is the traditional method of sure diagnosis with 15-30% false negative results [11].

Nitrazine paper test may lead to false negative or positive results due to contaminated samples by semen, blood, alkaline urine, vaginitis or using antibiotics. Fern test also has 5-30% false positive and 15-30% false negative results [10].

Accurate diagnosis is achieved by demonstration of specific amniotic fluid markers in vaginal discharge. These tests include detection of α -fetoprotein, prolactin, di-amine oxidase, human chorionic gonadotropin, insulin like growth factor binding protein-1 (IGFBP-1), and fetal fibronectin. Most of these tests have the advantage of being accurate but expensive and time consuming with variable results [12]. The direction has been on studying urea and creatinine detection in cervicovaginal discharge. These studies declared accuracy of 90-100% to determine the PROM [13].

Urea and creatinine in the amniotic fluid are produce from fetal urine in second half of pregnancy. Urea plays an important role in the metabolism of nitrogen-containing substances and is the chief nitrogen-containing substance in the urine. Creatinine is a break-down product of creatinine phosphate in muscles and is usually produced at invariant rate and is mainly filtered out through the kidneys [14].

Kafali and Oksuzler [12] presumed that urea and creatinine in vaginal fluid may be helpful in PROM diagnosis because fetal urine is the main source of amniotic fluid in the second half of pregnancy.

This study was conducted to evaluate the diagnostic value of vaginal wash urea and creatinine levels in patients with PROM. The study was carried out at the Department of Obstetrics and Gynecology, Zagazig University Hospitals. A total of 228 pregnant women were included in study, between completed 24 weeks to completed 37 weeks' gestation, divided into two equal groups: 114 pregnant women with PROM and 114 pregnant women with no history of fluid leaking.

The study showed that there is non-significant difference between both groups regarding age, BMI, onset of leakage, gestational age, gravidity, parity, history of miscarriage, blood pressure, respiratory and heart rates and temperature, but there is statistically significant difference between the studied groups regarding AFI.

Kariman et al. [5] evaluated the vaginal fluid urea and creatinine reliability for PROM diagnosis. A total of 179 pregnant women were included in the study. The first group consisted of 126 pregnant women between 14-41 weeks' gestation with history of vaginal fluid leakage. Patients who had visual pooling, positive nitrazine paper and fern test results were considered as confirmed PROM (Group 1). While patients without visual pooling, negative nitrazine paper and fern test results were

taken as suspected unconfirmed PROM cases (Group 2). The control group consisted of 53 pregnant women with no leaking complaint or complication (Group 3). Age, parity, gravidity and gestational age were compared with analysis of variance between groups.

Our study found a statistically significant difference between the two groups concerning vaginal wash urea. The best cutoff value of vaginal wash urea in prediction of PROM is ≥ 6.85 mg/dl with AUC of 0.958, sensitivity of 98.2%, specificity of 70.2%, PPV of 76.7%, NPV of 97.6% and accuracy of 93%.

Kafali and Oksuzler [12] found that mean vaginal fluid urea levels in definite PROM, suspected PROM and control groups were 34.6 ± 5.3 mg/dl, 2.4 ± 5.3 mg/dl and 1.3 ± 6.2 mg/dl respectively, where the difference was statistically significant ($p < 0.01$) with sensitivity, specificity, positive predictive value, and negative predictive value were 100% for all and cut off value of 12mg/dl.

Tita and Andrews [15], evaluated vaginal fluid urea concentration and found that the mean vaginal fluid urea levels in confirmed PROM, suspected PROM and control groups were 9.04 ± 0.57 , 4 ± 0.31 and 3.3 ± 1.7 mg/dl respectively, where the difference was statistically significant ($p < 0.05$). The sensitivity, specificity, and positive and negative predictive value were 100%, 76.5%, 70.6% and 96%, respectively and cut off value of 3.5mg/dl.

Also, David et al. [16] found that mean vaginal fluid urea levels in confirmed PROM and control group were 27.6 ± 6.2 mg/dl and 1.1 ± 2.7 mg/dl respectively, where the difference was statistically significant (p -value < 0.05) with sensitivity, specificity, positive predictive value, and negative predictive value were 83%, 97.3%, 96.5% and 85.6% respectively and cut off value of 9.6mg/dl.

Kariman et al. [5] studied the mean concentration of vaginal wash fluid urea in confirmed PROM, suspected PROM and control groups. The mean urea levels in vaginal wash fluid in group 1, 2 and 3 were 13.77 ± 5.41 mg/dl, 4.71 ± 3.64 mg/dl and 5.13 ± 5.97 mg/dl respectively with statistically significant differences ($p < 0.001$). The area under the curve is 84% for urea. The optimal cut-off value for urea is 6.0mg/dl with sensitivity of 90%, specificity of 79%, positive predictive value of 83%, negative predictive value of 87.5% and accuracy of 85% were found.

Our study showed that there is a statistically significant difference between the two groups

regarding vaginal wash creatinine. The best cutoff value of vaginal wash creatinine in prediction of PROM is ≥ 0.465 with AUC of 0.992, sensitivity of 100%, specificity of 80.7%, PPV of 83.8%, NPV of 100% and accuracy of 90.4%.

Li et al. [17] found that creatinine detection in vaginal wash fluid is easier and less expensive than hCG & AFP and appears to be more accurate than hCG in diagnosing PROM. The study group involved 54 women in their 3rd trimester of pregnancy with confirmed PROM and the control group involved 34 pregnant women without PROM. The vagina was washed by 3ml of saline solution injected by syringe, and the collected fluid was taken for creatinine quantitative assay. The results statistics were with a significant level of $p < 0.05$.

These results cope with the results of Harita et al. [18] in evaluation of creatinine concentration in vaginal wash fluid for PROM detection, where sensitivity, specificity, negative predictive value, and positive predictive value were 94%, 90%, 88.6% and 100% respectively and cut off value of 0.55mg/dl.

Gurbuz et al. [19] showed that creatinine detection in vaginal wash fluid is a useful marker in suspected cases of PROM. In these cases, new methods such as fetal fibronectin, β -hCG and AFP were investigated. However, because of values overlap in patients with ruptured and intact membranes, they have low specificity. The creatinine assay is excelled in being fast and cheap with high accuracy to establish diagnosis. It is likely to be a ideal test for PROM diagnosis by evaluation of vaginal fluid creatinine concentration with sensitivity, specificity, positive predictive value, and negative predictive value were 100% for all.

Kafali and Oksuzler [12] found that mean creatinine levels of vaginal wash fluid of definite PROM, suspected PROM and control groups were 1.5 ± 0.3 mg/dl, 0.34 ± 0.22 mg/dl and 0.28 ± 0.23 mg/dl respectively, where the differences were statistically significant (p -value < 0.01) with sensitivity, specificity, positive predictive value, and negative predictive value were 100% for all and cut off value of 0.6mg/dl.

Also, Tita and Andrews [15] found that the mean creatinine level of vaginal wash fluid of confirmed PROM, suspected PROM and control groups were 0.82 ± 0.05 , 0.55 ± 0.04 and 0.07 ± 0.02 mg/dl respectively, where the differences were statistically significant ($p < 0.05$). The sensitivity, specificity and positive and negative predictive values were

90.2%, 91.2%, 83.6% and 90% respectively with a cut off value of 0.75mg/dl.

Kariman et al. [5] demonstrated that creatinine has the higher diagnostic power with the mean creatinine level in vaginal wash fluid among confirmed PROM, suspected PROM and control groups were 1.58 ± 1.01 mg/dl, 0.36 ± 0.23 mg/dl and 0.22 ± 0.10 mg/dl respectively. The differences between groups were statistically significant ($p < 0.001$). The area under the curve for creatinine is 99.99%. From the ROC curve, 0.45mg/dl was set as a cut-off value for creatinine. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 100% for all.

A study was carried out by Mohamed and Mostafa [20] for detecting PROM by evaluation of vaginal urea and creatinine concentration. The sensitivity, specificity, positive predictivity and negative predictivity were 100% for all with cut-off values of 13.2mg/dl and 0.31mg/dl respectively.

In our study, combined use of vaginal wash urea and creatinine in prediction of PROM had sensitivity of 98.3%, specificity of 91.2%, PPV of 91.8%, NPV of 98.1%, accuracy of 94.7%.

Kafali and Oksuzler [12] have found that determination of vaginal wash fluid urea and creatinine for the diagnosis of PROM was a simple, reliable, inexpensive and rapid test. Creatinine values in the amniotic fluid stand for fetal maturity. A creatinine concentration of ≥ 1.75 mg/dl correlates significantly with a gestational age of 37 weeks or more, which confirmed renal maturation.

Our study showed that urea and creatinine assays are cheap and fast methods with high sensitivity and specificity to establish accurate diagnosis. It is possible to be a gold standard test for PROM as it is cheaper, faster with higher sensitivity and specificity than α -FP, β -HCG and fetal fibronectin.

Oliveira et al. [21] found a significant correlation between gestational age and amniotic fluid creatinine ($r > 0.85$, $p < 0.01$). Meanwhile, Creatinine concentrations in amniotic fluid increased gradually between 20-32 weeks of gestation and more rapidly thereafter, when they were two to four times higher than in maternal serum.

Osman and Elghazaly [22] evaluated the accuracy of urea and creatinine in vaginal wash fluid for diagnosis of PROM and found that they are accurate, inexpensive and simple tests for diagnosis of PROM.

Gezer et al. [23] concluded that measurement of urea and creatinine levels in vaginal wash fluid in cases of PPRM is a reliable and rapid test for diagnosis and also for delivery interval prediction after PPRM.

Conclusion: This study concluded that urea and creatinine assay is cheaper, faster and more valid (has higher sensitivity and specificity) than other vaginal fluid markers as α -fetoprotein, human chorionic gonadotropin and fetal fibronectin to establish accurate diagnosis of PROM. In the present series, the simplicity and the availability of this test make it easier in clinical practice. So, vaginal fluid creatinine and urea are possible candidates to become an ideal test for diagnosis of PROM. The study also recommended application of these new tests as a routine investigation in diagnosis of PROM in a large scale of population.

Ethics approval and consent to participate: Institutional review board's approval of Zagazig University was obtained and written informed consent was taken from all patients.

Consent for publication: Consent was obtained from all patients regarding participation and publication of the study results with all respect to confidentiality. All authors accept the publication.

Availability of data and material: Data was recruited from cases attending obstetric outpatient clinics of Zagazig University Hospitals.

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Authors' contributions: All authors participated in sampling, data collection, intervention and statistical analysis. All authors have read and approved the manuscript.

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تقييم اليوريا والكرياتينين في سائل الغسيل المهبل كوسيلة لتشخيص تمزق أغشية السلوى المبكر

مقدمة: (PROM) تشير إلى تمزق أغشية الجنين قبل بداية المخاض بعد 37 أسبوع من الحمل، أما لو حدث ذلك قبل 37 أسبوع فيسمى (PPROM) يرتبط طول المدة من التمزق حتى الولادة بزيادة الاعتلال للأمهات والمواليد مكتملي النمو والخدج، ويشمل هذا التهاب السائل والغشاء الأمنيوسي، انتان المواليد، انفصال المشيمة، الولادة المبكرة، هبوط الحبل السرى، وزيادة معدل الولادة القيصرية. النساء الحوامل اللاتي لديهن تاريخاً بتسريب سائل من المهبل أو شخصن عن طريق الموجات فوق الصوتية بنقص السائل الأمنيوسي يجب تقييمهن بعناية لتجنب النتائج السلبية. يساعد التشخيص الدقيق الأطباء على تحسين نتائج الأمهات والمواليد من خلال التدخل المبكر لتقليل الاعتلال. تشخيص PROM قد يكون سهلاً عن طريق رؤية التسرب من خلال عنق الرحم أو تراكم السائل أثناء فحص المنظار. ولكن مع تمزق الغشاء الصغير أو تمزق الكيس الخلفي قد يكون من الصعب تشخيص التسرب، مما قد يؤدي إلى تأخر التشخيص والعلاج. وتشمل طرق تشخيص PPRM اختبار السرخس والنيترازين وهما اختباران شائعاً الاستخدام وتقليديين. ويمتازا بالسرعة والسهولة ولكن لا يمكن الاعتماد عليهما تماماً بسبب ارتفاع النتائج الإيجابية والسلبية الخاطئة، والتي قد تكون ذات صلة بالأخطاء التقنية أو التلوث بالدم، السائل المنوي أو مخاط عنق الرحم. لا يمكن للتقييم بالموجات فوق الصوتية للسائل الأمنيوسي التمييز بين PROM والأسباب الأخرى لنقص السائل الأمنيوسي. ومع ذلك، فإن اختبار السدادات القطنية والصبغة هو اختبار للتشخيص الدقيق من خلال حقن صبغة في السائل الأمنيوسي تحت توجيه الموجات فوق الصوتية. وهو اختبار يحمل خطر النزيف، العدوى، انفصال المشيمة، الإجهاض، وثقب الرحم. اختبار الـ Amnisure لتشخيص ROM دقيق ولكنه مكلف وغير متوفر في العديد من المراكز. وبالتالي، فهناك حاجة إلى طريقة بسيطة و آمنة وغير مكلفة للكشف عن PROM. تفرز اليوريا والكرياتينين عن طريق الكلى ويحتوي السائل الأمنيوسي أيضاً على هذه المواد ويمكن استخدامها في المهبل كاختبار تشخيصي لـ PROM.

الهدف من الدراسة: أجريت هذه الدراسة لبحث القيمة التشخيصية لمستويات اليوريا والكرياتينين في سائل الغسيل المهبل في المرضى الذين يعانون من اشتباه بـ PROM.

الحالات وطرق الدراسة: أجريت الدراسة في قسم أمراض النساء والتوليد بمستشفيات جامعة الزقازيق. وشملت الدراسة 228 امرأة حامل بين 24 أسبوعاً إلى 37 أسبوعاً مكتملاً، قسمن إلى مجموعتين متساويتين: المجموعة A مع PROM مؤكد، مجموعة التحكم هي B. خضعت جميع النساء الحوامل المشمولات في هذه الدراسة إلى: أخذ التاريخ الكامل، الفحص العام، فحص البطن والمنظار، اختبار السرخس، اختبار النيترازين. قياس اليوريا في سائل غسيل المهبل يقاس عن طريق أنزيم urease أما الكرياتينين فيقاس بطريقة RATE JAFFE.

النتائج: أظهرت الدراسة أن هناك فرقاً إحصائياً ملحوظاً بين المجموعتين فيما يتعلق باليوريا والكرياتينين في سائل غسيل المهبل. أفضل قيمة قطعية لليوريا في التنبؤ بـ PROM هي $6.85 \leq$ مجم/دل مع AUC 0.958، حساسية 98.2%، خصوصية 70.2%، قيمة تنبؤية إيجابية 76.7%، قيمة تنبؤية سلبية 97.6% ودقة 93%. أفضل قيمة قطعية للكرياتينين للتنبؤ بـ PROM هي $0.465 \leq$ مجم/دل مع AUC 0.992، حساسية 100%، خصوصية 80.7%، قيمة تنبؤية إيجابية 83.8%، قيمة تنبؤية سلبية 100%، ودقة 90.4%. وكان للاستخدام المشترك لليوريا والكرياتينين في التنبؤ بـ PROM حساسية 98.3%، وخصوصية 91.2%، قيمة تنبؤية إيجابية 91.8%، قيمة تنبؤية سلبية 91.8% ودقة 94.7%.

الاستنتاج: خلصت هذه الدراسة إلى أن فحص اليوريا والكرياتينين في السائل المهبل أرخص وأسرع وأكثر دقة، وهو مرشح محتمل لكونه اختباراً قياسياً ذهبياً لتشخيص PROM.