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MAPPING THE LEVELS OF CREATININE, UREA, AND BETA hCG IN VAGINAL FLUIDS

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ABSTRACT

Background: Beginning in the eighth to tenth week of pregnancy, urine excretion in amniotic fluid is the basis for the use of creatinine and urea in the diagnosis of PROM. The syncytiotrophoblast secretes B-hCG (beta-human chorionic gonadotropin), which is found in mother's blood and amniotic fluid and is being researched for its evolutionary significance.

Aim: to map the levels of beta-hCG, urea, and creatinine in vaginal fluids in order to determine premature rupture of the membranes, or PROM.

Methods: The study evaluated women who were split into two groups. Group I included pregnant women who were 28–40 weeks along, had a positive history of vaginal leakage without the beginning of labor pain, and were clinically diagnosed with PROM. Group II consisted of control pregnant women without PROM who were between the ages of 28 and 40 weeks. These two groups were compared for the levels of creatinine, urea, and beta hCG in vaginal fluids.

Results: The baseline demographic information for the two research groups was similar. The levels of urea, beta-hCG, and creatinine in vaginal fluids were found to be considerably higher in the study group. For creatinine in vaginal fluid, the sensitivity, specificity, and cut-off values were 86.65%, 48.1%, and >0.08, respectively. The urea levels in vaginal fluid were 63.31%, 98.1%, and >3.4 IU/L. For β -hCG in vaginal fluids, the sensitivity, specificity, and cut-off values were 95%, 83.1%, and >9 mg/dl, respectively.

Conclusions: a quick, accurate, and easy way to diagnose PROM is to look for creatinine, urea, and β -hCG in vaginal fluid. Because it has been shown to be a practical, affordable, and viable test, it should be included in routine examinations even at community-level clinics with limited resources.

Keywords: β -hCG, creatinine, urea, PROM, premature rupture of membranes, vaginal fluid

INTRODUCTION

Premature rupture of membrane, or PROM, is a condition that occurs when the fetal membrane ruptures before labor begins, regardless of the female's gestational age. The accumulation of fluid in the posterior fornix after evaluating the speculum and history of watery discharge per vaginum is the cornerstone for the diagnosis of PROM. Premature rupture of membrane, or PROM, can be overdiagnosed or underdiagnosed, which can lead to needless obstetric procedures and poor care, both of which can end in potentially fatal consequences for the mother and newborn.¹

The speculum examination's fluid buildup in the posterior fornix and the amniotic fluid's clear flow are used to make the first diagnosis of PROM.

When the pH indicator paper changes from yellow to blue, indicating that the amniotic fluid has a basic pH, PROM can also be identified with the Nitrazine test. A Fern test, which shows the microscopic appearance of a palm-leaf pattern in the dried amniotic fluid, is also used to identify PROM. Nevertheless, these three conventional approaches of evaluating the PROM are linked to a number of shortcomings.²

Fetal membranes are resilient throughout the early stages of pregnancy. The danger of these membrane ruptures increases as the pregnancy gets closer to term because the membranes weaken and their collagen concentration decreases. In addition, different fetal movements in the latter stages of pregnancy cause the uterus to contract and become more tense, which helps the membranes to burst at term. Nearly 2-4% of preterm pregnancies and 10% of all term pregnancies have PROM, which can result in infection in afflicted females and premature births.

Three patient histories provided in PROM have a reliability of around 10% to 50%, and speculum evaluation of fluid leaking from the cervix area is linked to approximately 12% to 30% of false negative outcomes. Additionally, the presence of any antiseptic agent, vaginitis, cervicitis, blood, semen, meconium, or urine in the cervicovaginal discharge can also interfere with correct findings because all of these substances are alkaline, which is why the Nitrazine test has a high probability of false positives.

False positive and false negative findings are also linked to the Fern test, which is used to evaluate PROM. Since the ultrasonography examination cannot distinguish PROM from other reasons for the reduction in liquor, the assessment of amniotic fluid may produce inaccurate results.⁴

Intra-amniotic dye injections are one of several invasive tests that provide a risk to both the mother and the fetus. The Amnisure ROM test is another method for evaluating PROM; it is quick, simple, and minimally intrusive, and it has good specificity and sensitivity. Nevertheless, Amnisure is a costly test that is unavailable in many Indian facilities. Data from earlier research has recently supported the measurement of creatinine, urea, and beta-hCG in the cervicovaginal fluid.

Since the fetus begins excreting urine in the amniotic fluid between weeks 8 and 11 of gestation, fetal urine makes up the majority of the amniotic fluid in the second half of pregnancy. This is the rationale for utilizing creatinine and urea to diagnose PROM. Only syncytiotrophoblasts release beta-hCG, which is detected in amniotic fluid as well as the mother's urine and blood, which are also examined for assessment.⁵ In order to detect PROM (premature rupture of membranes), the current study set out to map the levels of creatinine, urea, and beta hCG in vaginal secretions.

MATERIALS AND METHODS

The Institute's Department of Obstetrics and Gynecology is the site of the current cross-sectional observational clinical comparison investigation. Prior to their involvement in the study, all participants gave their written and verbal informed permission.

The 120 female participants in the study were split into two groups of 60 subjects each. Group I consisted of pregnant women in the 28–40 week gestational age range who had a history of vaginal leakage without the onset of labor pains and subjects who had been clinically diagnosed with premature rupture of membranes, or PROM. The controls, or Group II individuals, were pregnant women without PROM who were between 28 and 40 weeks along in their gestation.

Women who were willing to participate, had a single intrauterine pregnancy, and were between the ages of 28 and 40 weeks as established by reliable LMP (last menstrual period) and ultrasound-confirmed dates were all eligible to participate in the study.

Participants who presented with congenital malformations, irregular uterine contractions, intrauterine death, insulin-dependent diabetes mellitus or nephropathy, blood in vaginal discharge, placenta praevia, multiple pregnancies, or who did not consent to participate in the study were excluded from the study. Following the final inclusion of the research participants, a thorough history was obtained, and then each participant underwent a thorough general and abdominal examination as well as a sterile speculum examination to ensure that amniotic fluid was flowing from the cervix.

The collected fluid was placed on the pH paper after a cotton applicator tip was pushed deeply into the vagina. When the pH paper changed from yellow to blue, it was deemed that there was a leak of amniotic fluid from the research participants' cervix. 60 pregnant women in Group I reported having a vaginal leak, and a positive fluid leak on a pH paper test and sterile speculum inspection allowed for the clinical diagnosis of PROM. 60 pregnant women who had negative vaginal leakage, age

and gestational age matching, fluid discharge that was negative on sterile speculum evaluation, and no change in pH paper test were included in Group II.

Using the transabdominal sonography examination, a thorough evaluation of the participants' gestational age, amniotic fluid index, and fetal viability was conducted. After injecting 5 ml of sterile saline solution into the posterior vaginal fornix and withdrawing 3 ml using the same syringe, the vaginal aspirate was collected.

Before administering any medication or performing a vaginal examination, the sample process was carried out within six hours of the membrane rupturing. The collected samples were taken to the lab to measure the levels of urea, creatinine, and β -hCG. The electrochemiluminescence test was used to measure β -hCG. Jaffe's technique was used to measure creatinine levels, while the enzymatic urease method was used to measure urea levels. A preformed, structured, pretested proforma was used for the assessment of various variables such as demographic data, obstetrics characteristics, ultrasonographic findings of AFI, β -hCG, urea, and creatinine levels, pH test, and results of sterile speculum examination.

The data gathered were analyzed statistically using the SPSS software version 21.0 (IBM Corp., Armonk, NY, USA) and unpaired t-test with the chi-square test. The data were expressed as mean and standard deviation and frequency and percentage. Statistical significance was kept at a p-value of <0.05 .

RESULTS

The 120 female participants in the study were split into two groups of 60 each. Group I consisted of pregnant women between 28 and 40 weeks of gestation who had a history of vaginal leakage without the onset of labor pains and who were clinically diagnosed with premature rupture of membranes, or PROM. The controls, or Group II individuals, were pregnant women without PROM who were between 28 and 40 weeks along in their gestation. In terms of demographics, the research participants in Groups I and II had mean ages of 29.90 ± 3.37 and 26.30 ± 2.98 years, respectively. 64% and 51% of the research participants in Group I and II, respectively, were between the ages of 36 and 39.

Additionally, the majority of the participants in both groups were primigravida, indicating that there was no statistically significant difference between the two groups' baseline demographic characteristics. It was observed that the β -hCG levels in the two study groups were 6.25 ± 7.19 μ L in Group II participants without premature rupture of membranes and 282.11 ± 541.05 μ L in Group I subjects with PROM. Table 1 demonstrates that the levels were extremely statistically significant in PROM participants as compared to controls ($p=0.001$).

When urea levels in the two study groups were analyzed, it was shown that those in Group I who experienced premature membrane rupture had considerably higher urea levels (10.78 ± 12.74 IU/L) than those in Group II (1.09 ± 0.95 IU/L) that were from Group II (controls) without rupture of the membrane and the p-value of 0.001 as depicted in Table 2.

According to the research's findings, the creatinine levels in the vaginal fluid of study participants from Group I (PROM subjects) were 0.68 ± 0.74 mg/dl, greater than those of Group II (control) people who did not have PROM, which were 0.23 ± 0.27 mg/dl. Table 3 summarizes the difference between the two groups, which was statistically significant with $p=0.001$.

Additionally, Table 4 shows that when the amniotic fluid index (AFI) was compared between the two study groups, it was significantly lower in Group I subjects who experienced premature membrane rupture (06.67 ± 2.09) than in Group II (control) subjects who did not experience premature membrane rupture (10.12 ± 3.00) ($p=0.001$).

For creatinine in vaginal fluid, the sensitivity, specificity, and cut-off values were 86.65%, 48.1%, and >0.08 , respectively. The urea levels in vaginal fluid were 63.31%, 98.1%, and >3.4 IU/L. For β -hCG in vaginal fluids, the sensitivity, specificity, and cut-off values were 95%, 83.1%, and >9 mg/dl, respectively.

RESULTS

In this study, 120 females were evaluated and split into two groups of 60 subjects each. Group I consisted of pregnant women between 28 and 40 weeks of gestation who had a history of vaginal leakage without the onset of labor pains and who were clinically diagnosed with premature rupture of membranes, or PROM. Group II people, or controls, were pregnant women between weeks 28 and 40 of pregnancy who did not have PROM.

In terms of demographics, the average age of the research participants in Groups I and II was 29.90 ± 3.37 years and 26.30 ± 2.98 years, respectively. 64% of research participants in Group I and 51% of study participants in Group II were between the ages of 36 and 39. Additionally, the majority of the participants in both groups were primigravida, indicating that there was no statistically significant difference between the two groups' baseline demographic characteristics. These findings corresponded

to those of the 2011 study by Knapik D et al. and the 2014 study by Palacio M et al., both of which used similar demographic data to evaluate their individuals.

When β -hCG levels were measured in the two study groups, it was found that Group I participants with PROM had β -hCG levels of $282.11 \pm 541.05 \mu\text{L}$, whereas Group II subjects without premature rupture of membranes had β -hCG values of $6.25 \pm 7.19 \mu\text{L}$. When comparing participants with PROM to controls, the levels were significantly statistically significant ($p=0.001$). The present study's results were in line with those of Borg HM et al. (2019) and Bouzari Z et al. (2018), who found that participants with preterm rupture of membranes had considerably higher levels of β -hCG.

In order to compare the urea levels in the two research subject groups, Urea levels were found to be substantially greater in Group I participants with premature membrane rupture ($10.78 \pm 12.74 \text{ IU/L}$) than in Group II (controls) subjects without membrane rupture ($1.09 \pm 0.95 \text{ IU/L}$), with a p-value of 0.001. These results were consistent with those of Kuruoglu YS et al. (2011) and Ghasemi M et al. (2016), who found that females with PROM had higher urea levels.

When the creatinine levels in the study participants' vaginal fluid were analyzed, it was found that Group I (PROM subjects) had greater creatinine levels ($0.68 \pm 0.74 \text{ mg/dl}$) than Group II (control) individuals (who did not have PROM; their creatinine levels were $0.23 \pm 0.27 \text{ mg/dl}$).

The difference was statistically significant in the two groups with $p=0.001$. these results were in line with Garg R et al¹² in 2019 and El-Garhy IT et al¹³ in 2019 where authors reported significantly higher levels of creatinine in subjects with PROM compared to females without PROM.

When the amniotic fluid index (AFI) of the two study groups was compared, it was found that Group I subjects with premature membrane rupture had a significantly lower AFI (06.67 ± 2.09) than Group II (control) subjects without premature membrane rupture (10.12 ± 3.00 ; $p=0.001$). For creatinine in vaginal fluid, the sensitivity, specificity, and cut-off values were 86.65%, 48.1%, and >0.08 , respectively. The urea levels in vaginal fluid were 63.31%, 98.1%, and $>3.4 \text{ IU/L}$. For β -hCG in vaginal fluids, the sensitivity, specificity, and cut-off values were 95%, 83.1%, and $>9 \text{ mg/dl}$, respectively. These findings aligned with earlier research by Jain S et al. (2014) and Neil PR et al. (2010), which found that sensitivity, specificity, cut-off values, and AFI were similar to our study.

CONCLUSIONS

Given its limitations, the current study comes to the conclusion that a quick, accurate, and easy way to diagnose PROM is to look for creatinine, urea, and β -hCG in vaginal fluid. Because it has been shown to be a practical, affordable, and viable test, it should be included in routine examinations even at community-level clinics with limited resources. However, further longitudinal research is required to fully examine the problem.

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Groups	β -hCG levels (Mean $\pm$ S. D)	p-value
PROM (I)	282.11 $\pm$ 541.05	0.001
Controls (II)	6.25 $\pm$ 7.19	

Table 1: Comparison of β -hCG levels in the two groups of study subjects

Groups	Urea levels (Mean $\pm$ S. D)	p-value
PROM (I)	10.78 $\pm$ 12.74	0.001
Controls (II)	1.09 $\pm$ 0.95	

Table 2: Comparison of urea levels in the two groups of study subjects

Groups	Creatinine levels (Mean $\pm$ S. D)	p-value
PROM (I)	0.68 $\pm$ 0.74	0.001
Controls (II)	0.23 $\pm$ 0.27	

Table 3: Comparison of creatinine levels in the two groups of study subjects

Groups	AFI (Mean $\pm$ S. D)	p-value
PROM (I)	06.67 $\pm$ 2.09	0.001
Controls (II)	10.12 $\pm$ 3.00	

Table 4: Comparison of AFI (amniotic fluid index) in the two groups of study subjects