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DETECTION OF PREMATURE RUPTURE OF MEMBRANES WITH THE HELP OF VAGINAL FLUID CREATININE IN PATIENTS ADMITTED AT GUJARAT ADANI INSTITUTE OF MEDICAL SCIENCE, BHUJ, GUJARAT, INDIA- A OBSERVATIONAL STUDY

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ABSTRACT

Aim: The aim of present study was to estimate the reliability of vaginal fluid creatinine for the analysis of premature rupture of membranes. **Material and Methods:** A total of 180 pregnant women were recruitedin the study. Group I (confirmed group) consisted of 60 women with a diagnosis of rupture of membranes established by visualization of fluid passing from the cervical canal. Group II (suspected group) consisted of 60 women with a complaint of vaginal fluid escape but without clear amniotic fluid flowing from the cervix or vaginal pooling with negative nitrazine test. The control group (group III) consisted of 60 women without any complaint or complication. All patients were sampled for vaginal fluid creatinine by speculum examination. One-way ANOVA, c2, and Kruskal-Wallis test, as well as receiver operating characteristic (ROC) curve analysis were used. Analysis was done with SPSS version 15. The level of significance was set at 0.05 and confidence interval was set at 95%. **Results:** The mean vaginal fluid creatinine in groups I, II, and III were 1.74 ± 0.8, 0.45 ± 0.2 and 0.25 ± 0.1 mg/dL, respectively. The creatinine level was significantly superior in the confirmed group (group I) than in the other two groups ($P < 0.001$). The optimal cut-off value was 0.5 mg/dL with 96.7% sensitivity, 100% specificity, 100% positive predictive value, and 96.8% negative predictive value. **Conclusion:** Vaginal fluid creatinine determination for the diagnosis of PROM is reliable, simple, rapid and inexpensive.

KEYWORDS: Creatinine, Diagnosis, Vaginal fluid, Women.

INTRODUCTION

Premature rupture of membranes (PROM) occurs in 10% of all pregnancies and is a chief cause of preterm birth and perinatal morbidity and mortality.[1] Correct diagnosis of PROM is crucial for suitable management and requires a sensible evaluation of history, clinical findings and specialized tests. Failure to identify patients or false-positive finding of membrane rupture may lead to wrong management and serious maternal/neonatal complications or unnecessary obstetric interventions. The diagnostic tests presently used in clinically asymptomatic or suspicious cases include measurement of vaginal pH, alpha fetoprotein (AFP), human chorionic gonadotropin (hCG), diamine oxidase, prolactin, insulin growth factor binding protein-1 (IGFBP-1), fetal fibronectin and fern test. However, none of these tests analyze or eliminate rupture of membranes (ROM) with certainty.[2–6] Knowing that fetal urine is the most significant source of amniotic fluid in the third trimester, in recent years some studies have recommended measurement of creatinine in vaginal fluid for the diagnosis of ROM.[7–9] The current study evaluates the reliability of creatinine measurement for the diagnosis of ROM admitted to Gujarat adani institute of medical science, Bhuj, Gujarat, India.

MATERIAL AND METHODS

One hundred and ninety-two pregnant women with a singleton pregnancy and gestational age (GA) of 28–40 weeks who were admitted to Gujarat adani institute of medical science, Bhuj, Gujarat, India were recruited into this study. The study was approved by the ethics committee of Gujarat adani institute of medical science and informed consent was taken from all the participants. The study group consisted of 132 pregnant women with a complaint of vaginal fluid leakage (case group) and 60 normal pregnant women admitted to the prenatal clinic for regular prenatal control visits with no complaints or complications were selected randomly (control group). Twelve women in the first group were excluded from the study due to the occurrence of vaginal spotting/ bleeding, uterine contractions or medical/prenatal complications. GA was determined according to the ultra sound of the first half of pregnancy. All women in the first group

underwent a sterile speculum assessment to confirm amniotic fluid (AF) flowing from the cervix. Positive results were considered as 'confirmed PROM group' (group I), while patients with a complaint of vaginal fluid leakage and no obvious AF flowing or AF pooling with negative nitrazine test were consider as 'suspected PROM group' (group II). There were 60 participants in each group. Every single women underwent ultra sound examination for determination of AF and GA.

In cases of flowing/pooling AF, for creatinine sampling, vaginal fluid aspiration after injection of 3 mL of sterile water into the posterior vaginal fornix with the same syringe was performed, while in the control group, initially 5 mL of sterile water was injected into the posterior vaginal fornix; thereafter, 3 mL was aspirated with the same syringe. Samples were immediately sent to the Gujarat adani institute of medical science laboratory, centrifuged and kept refrigerated at -30°C.

All speculum examinations, sample collections, and ultra sound examinations were performed by the same physician. Age, parity, GA and creatinine level were compared using one-way ANNOVA and c2 test, while dilatation and effacement were compared using Kruskal-Wallis test. Receiver operating characteristic (ROC) curve analysis was used to establish an optimal cut-off point. Analysis was done with SPSS version 15. The level of significance was set at 0.05 and confidence interval was set at 95%.

RESULTS

Demographic data, clinical characteristics and vaginal fluid creatinine level in all three groups are shown in Table 1. The three groups were parallel with reverence to maternal age, parity, gestational age, dilatation, effacement and amniotic fluid index. The mean vaginal fluid creatinine concentration in group I was superior to the other two groups. Sensitivity, specificity, positive predictability and negative predictability in different cut-off values are presented in Table 2.

The sensitivity (96.5%), specificity (100%), positive predictive value (PPV) (100%) and negative predictive value (NPV) (96.8%) were uppermost in detecting PROM by evaluation of vaginal fluid creatinine concentration with a cut-off value of 0.5 mg/dL.

Table 1 Demographic data, clinical characteristics and vaginal creatinine levels of three groups of patients.

	PROM+ (Group I)	PROM? (Group II)	Control group	P-value
Maternal age (year ± SD)	26.7 ± 4.7	4.4 ± 26.1	4.3 ± 25.9	0.06
Parity	2.85 ± 1.05	1.1 ± 2.71	1 ± 2.93	0.7
Gestational age (w)	36.5 ± 3.5	37.5 ± 2.2	36.9 ± 2.3	0.9
Amnoitic fluid index (mm)	81.1 ± 30.2	89.2 ± 34.05	95 ± 28.1	0.10
Vaginal fluid creatinine (mg/dL)	1.74 ± 0.8	0.45 ± 0.2	0.25 ± 0.1	0.001*
Cervical dilatation (cm)	1.53 ± 0.21	1.48 ± 0.8	1.61 ± o.25	0.45
Cervical effacement (%)	27 ±3	31± 4.5	28 ± 4	0.21

*** indicates statically significant difference at p=0.05.**

Table 2 Vaginal fluid creatinine level (mg/dL)

	1	0.9	0.8	0.7	0.6	0.5	0.4
Sensitivity	78.3%	80.3%	85%	86.7%	90%	96.7%	86.7
Specificity	100%	100%	100%	100%	100%	100%	100%
Positive predictive value	100%	100%	100%	100%	100%	100%	100%
Negative predictive value	82.2%	83.3%	87%	88.2%	90.9%	96.8%	88.2%

DISCUSSION

Accurate and timely diagnosis of PROM is important for optimizing pregnancy outcome and management is based on correct diagnosis. Still, a non-invasive diagnostic gold standard is not available and the conventional non-invasive diagnostic methods, including pooling assessment, microscopic fern test and pH examination of cervicovaginal discharge, have restrictions in terms of cost, simplicity and diagnostic accuracy, especially with passage of time since membrane rupture. However, the gold standard for diagnosis of PROM, amnio-dye test, is invasive and carries risks of infection, abruption and abortion.[7]

In recent years, researchers have focused on detecting various biochemical markers in cervicovaginal discharge when ROM occurs. These markers include AFP, fetal fibronectin, IGFBP-1, prolactin, b-hCG, urea, lactate, placental alpha-microglobulin-1 and 2 and creatinine.[9]

Li HY et al.[7] found that measurement of creatinine in vaginal fluid is cheaper and easier than hCG. In one more study Gurbuz et al.[8] reported that dimension of vaginal fluid creatinine with a cut-off value of 0.12 mg/dL and sensitivity, specificity, NPV and PPV of 100% in detecting PROM, is cheaper and quicker than other methods. Kafali *et al*.[9] reported that determination of urea or creatinine in vaginal fluid for the diagnosis of PROM is a reliable, simple and rapid test with sensitivity, specificity, NPV and PPV of 100% with a cut-off value of 12 and 0.6 mg/dL, respectively. They

speculated that analysis of vaginal creatinine and urea can be used as fetal maturation test in cases of preterm labor as creatinine level of AF depends on gestational ages.

The results of the present study, comparable to those by Kafali *et al*. showed that evaluation of vaginal fluid creatinine concentration with 96.5% sensitivity, 100% specificity, 100% PPV and 96.8% NPV with a cut-off value of 0.5 mg/dL is a valid and simple test, especially considering that it costs much less than hospitalization or other tests, such as placental alphamacroglobulin- 1 with similar sensitivity and specificity in suspicious cases.

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