Study of Vaginal Fluid- Creatinine Value for Diagnosis of Premature Rupture of Membranes

G.B. Madhavi[1], Karne Himavarshini[2]

ABSTRACT

Introduction: Premature rupture of fetal membranes (PROM) refers to rupture of fetal membranes before onset of labor. The aim of the study is to evaluate the reliability of vaginal fluid creatinine level in diagnosis of premature rupture of membranes.

Materials and methods: This was the prospective case control study of pregnant women having gestational age of 28 to 40 weeks who presented to department of Obstetrics and Gynecology at Chalmeda anand rao institute of medical sciences, Karimnagar from January 2020 to July 2022. They were divided into two equal groups : study group included 50 pregnant women who had z complaints of leaking per vaginum and control group with fifty pregnant women who had term delivery.

Results: The demographic data of both groups were comparable at the time of sampling. The accuracy of vaginal fluid creatinine with a cut off value >0.4mg/dl to diagnose PROM is more than 90%. The sensitivity ,specificity, positive predictive value ,negative predictive value and accuracy of amniotic fluid index to diagnose PROM were 97.80%,100.00%,100%,97.70% respectively with a cut-off value of ≤6. The sensitivity,specificity,Positive predictive value,Negative predictive value and accuracy of vaginal fluid creatinine to diagnose PROM were 99.89%,100.00%,100%,95.99% respectively with a cut-off value of >0.3 .

Conclusion: Vaginal fluid creatinine is a simple, practical, cost effective and easily accessible test and its incorporation with the low resource setting will be a game changer in the diagnosis of PROM.

Keywords: Creatinine, Premature Rupture of Membranes (PROM), Vaginal Discharge.

INTRODUCTION

Preterm PROM (PPROM) refers to rupture of fetal membrane before completing 37 weeks of gestation[1]. Definitive diagnosis of PROM is very important because failure of diagnosis or failure to identify patient or false positive diagnosis of PROM may lead to unwanted obstetrics complications such as placental abruption[1,] cord prolapse, chorioamnionitis [2] and serious maternal and neonatal complications. PROM is seen in 10% of term pregnancies and 2-4% of preterm pregnancies[3]. About one-third of women with PPROM develop potentially serious infections, such as septicemia[1], endometritis. Three gold standard documental clinical signs to diagnose rupture of membranes depend on clinical ability on sterile speculum examination: (1) visual pooling of clear fluid in the posterior fornix of vagina or leakage of fluid from cervical os. (2) Observation of transition from yellow to blue with PH indicator paper due to basic amniotic fluid flow (nitrazine test). (3) Detection of palm leaf pattern in dried amniotic fluid in microscopic method (fern test). The fetus and neonate are more affected with PPROM related morbidity and mortality than the mother did. Preterm infants are vulnerable to many problems, such as respiratory distress syndrome, intra-ventricular hemorrhage, periventricular leukomalacia, infection (eg, sepsis, pneumonia, meningitis), and necrotizing enterocolitis. There is a significant risk of maldevelopment of the alveolar tree (pulmonary hypoplasia) as well as fetal compression resulting in malformations similar to those on Potters syndrome with prolonged oligohydramnios[3]. The management of PROM is still controversial, hence it is important to reach accurate diagnosis by identifying the specific amniotic fluid markers in the vaginal fluid, measurement of fetal fibronectin, expensive but accurate and time consuming[4].

Vaginal creatinine may be helpful in diagnosis of PROM because fetal urine is the most important source of amniotic fluid in the second half of pregnancy[4].

In the presence of PROM the level of these fetal originated markers should be higher in the amniotic fluid than in normal cervicovaginal secretions Duff 1996 [5]

Study aimed to determine the vaginal fluid creatinine value for diagnosis of premature rupture of membranes in patients attending OBG department of CAIMS by using biochemical tests and to find of the strength of association.

MQTERIAL AND METHODS

It was a prospective, case control study in determination of vaginal fluid creatinine value for diagnosis of premature rupture of membranes. The study is carried out at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar in the department of Obstetrics and Gynecology among 100 patients from January 2020 to July 2022. Here 50 pregnant women who have complaints of leaking per vaginum and

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How to cite this article: Madhavi GB, Himavarshini K. Study of vaginal fluid- creatinine value for diagnosis of premature rupture of membranes. International Journal of Contemporary Medical Research 2021;8(9):I1-I4.

DOI: http://dx.doi.org/10.21276/ijcmr.2021.8.9.13

diagnosed as PROM will be compared with 50 pregnant women who were negative for amniotic fluid pooling on cusco speculum examination and delivered term.

It was approved by the ethical committee of obstetrics and gynecology, at Chalmeda anand rao institute of medical sciences, Karimnagar for all pregnant women who were included in this study, explanation of the study procedures was done and informed consent was obtained.

Inclusion criteria

Women with singleton live pregnancy with age group of 20-34 years with gestational age of 28-40 weeks [by LMP or 1st trimester sonography finding].

Pregnant women with high risk for PROM as pre mature rupture of membranes in a prior pregnancy, past history of preterm labor, pregnant women that reported a constant vaginal fluid leakage or a sensation if wetness within the vagina or the perineum were selected.

Exclusion criteria

In this study, pregnant women were excluded if there was pregnancy induced – hypertension or preeclampsia, liver or kidney disease, with vaginal spotting or bleeding or meconium in the vaginal fluid leak or recent vaginal infection having history of use vaginal drugs, women with presence of regular uterine contractions or fetal congenital anomalies or intra uterine fetal death or women with known medical and prenatal complications and any conditions that may have an impact on vaginal fluid creatinine concentration .

Study methodology

All participants were provided with a standard proforma which includes:

(I) - Detailed history including personal history as name, age, occupation,address and addictions. History of present pregnancy including a constant vaginal fluid leakage or a sensation of wetness within the vagina or the perineum, direct abdominal trauma, persistent headache, blurring of vision, lower abdominal pain, and any painless fresh bleeding . Menstrual history as last menstrual period to calculate expected date of delivery and gestational age. Obstetric history including parity, mode of previous delivery, previous history of preterm labor or PPROM . Past history for any comorbidities, blood transfusions, allergy to drugs, and surgeries. Family history for disorders (hypertension, diabetes mellitus),consanguinity, congenital fetal malformations.

(II) - Clinical examination including general examination: blood pressure to exclude hypertension, mainly temperature to exclude infection and abdominal examination for clinical estimation of liquor.

Vaginal examination with sterile Cusco speculum was done to exclude vaginal bleeding and then for vaginal fluid sampling.

(III) - Pelvic ultrasound examination was conducted with same ultrasound machine(PHILLIPS AFFINITI G) for all cases for determination of gestational age, amniotic fluid index and detection of fetal viability and congenital anomalies.

Methods: Patients examined in lithotomy position with a sterile Cusco speculum . After giving an informed consent, 5 ml of sterile saline solution was pooled into the posterior vaginal fornix using a sterile syringe, and 3 ml of the pooled saline was aspirated with the same syringe, then sent immediately to laboratory of Biochemistry Department at Chalmeda Anand Rao institute of medical sciences, for assay of creatinine (by spectrophotometer 5010 supplied by RANDOX laboratories ltd. UK) using JAFFE'S (KINETIC) S method. The concentration of creatinine was read by spectrophotometer at wave length 520 nm . Assessment of amniotic fluid index (AFI) is done by using four-quadrant technique[6] for each subject of the study. The AFI is considered normal between 8.1 and 18, low between 5.1 and 8, very low ≤ 5, high > 18 .

Subjects included in this study were divided into two groups: confirmed PROM group and normal non PROM group. Subjects who were positive for amniotic fluid pooling in the posterior vaginal fornix during a sterile Cusco speculum vaginal examination, on fundal examination they had lower gestational age than expected by date and had lower amniotic fluid index by ultrasound and they were taken as "confirmed PROM group".

Subjects who were negative for amniotic fluid pooling in the posterior vaginal fornix during a sterile Cusco speculum vaginal examination, had same gestational age on clinical examination corresponding to that expected date and had normal amniotic fluid index by ultrasound at time of obtaining the sample and were taken as " non PROM group. The parameters of maternal age, gestational age, parity,fetal presentation, and vaginal fluid creatinine levels were documented and compared between both groups.

For an optimal cut-off concentration Receiver operating characteristic (ROC) curve analysis has been .Results were evaluated with a significance level of $P < 0.05$.

RESULTS

In 68% women with PROM, AFI was <6 and 1% of the control. In the study observed that the mean concentration of creatinine was 0.66+/-0.19 mg/dl in the case group and 0.23+/-0.11 mg/dl in the control group, which was statistically significant (p<0.001).

In our study, mean AFI in women with PROM and control group were 5.16+/-1.98 and 9.56+/-2.45, respectively. In our study women with PROM had a decreased AFI, as observed which was statistically highly significant (p=0.001).

In our study, 97% of women belonging to control group have vaginal fluid creatinine levels <0.3mg/dl, while 1% of women with PROM have same value of vaginal fluid creatinine level. 3% of women belonging to control group have >0.3-0.6mg/dl of vaginal fluid creatinine levels while 42% of women with PROM have same values.0% women of control group and 45% of women with PROM have vaginal fluid creatinine levels in the range of >0.6-0.9mg/dl and 0% women of control group, 12% women with PROM have vaginal fluid creatinine value>0.9mg/dl.

Parameters	PROM(+) Group-1 (n=50)	PROM(-) Group-2 (n=50)	P Value
Maternal age	26.95+/-5.72	25.89+/-4.28(NS)	0.2967
Gestational age at sampling (wks)	34.65+/-4.95	35.48+/-4.40(NS)	0.3777
Primigravida	25%	35%	0.94
Multigravida	75%	65%	0.94

Table-1: The demographic characteristics of group

Parameter	PROM (+)	Control	p-value
Vaginal fluid creatinine level (mg/dl)	0.66±0.19	0.23±0.11	0.001
AFI(cm)	5.16±1.98	9.56±2.45	0.001

Table-2: Vaginal fluid creatinine leveL(mg/dl) AND AFI (cm) among groups

Parameter	Sensitivity	Specificity	PPV	NPV	Cutoff
AFI(cm)	97.80%	100.00%	100%	97.70%	≤6
Vaginal fluid creatinine(mg/dl)	99.89%	100.00%	100%	95.99%	>0.3

Table-3: ROC curve analysis

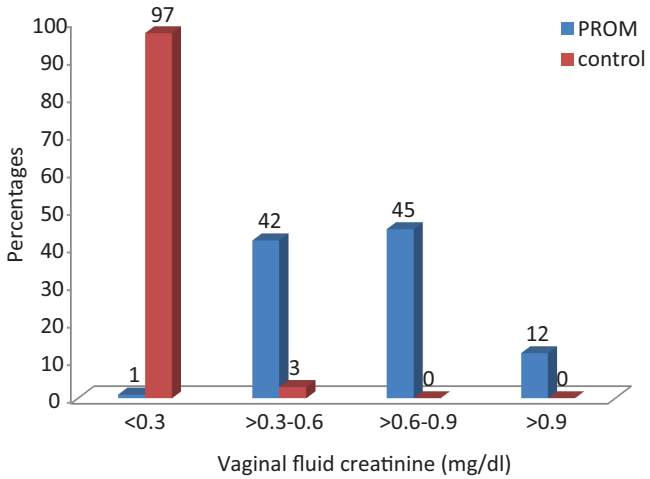

Figure-1: Distribution of women with prom and control group according to vaginal fluid creatinine

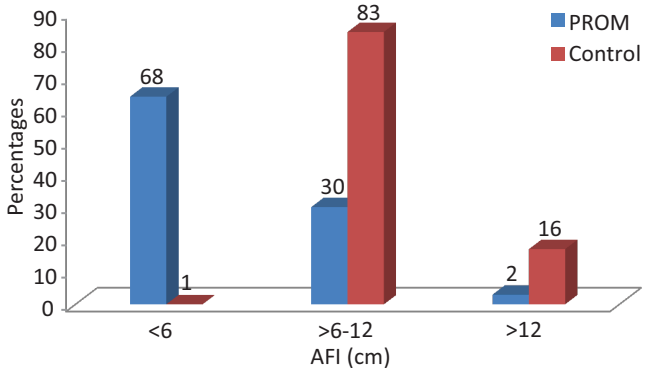

Figure-2: Distribution of women with prom and control group according to AFI

In our study, 68% of women with PROM have AFI value <6cm, while 1% of women of control group have value. 30% of women with PROM and 83% of control group have AFI value >6-12cm and 2% of women with PROM, 16% of women of control group have AFI >12cm.

DISCUSSION

In today's obstetrics PROM has been highly problematic. Confirmation of diagnosis plays an important role in initial management of PROM, Along with diagnosis,validating the gestational age, documenting fetal well being and deciding the mode of delivery is also important. To optimize the perinatal outcome and minimize the serious complications early and accurate diagnosis plays a vital role. A false diagnosis of PROM may sometimes lead to unnecessary obstetric intervention including inadvertent administration of antibiotics,corticosteroids, hospitalization, and even induction of labor.

In our study the accuracy of vaginal fluid creatinine with a cut off value >0.4mg/dl to diagnose PROM is more than 90%. The sensitivity,specificity, positive predictive value,negative predictive value and accuracy of amniotic fluid index to diagnose prom were 97.80%,100.00%,100%,97.70% respectively with a cut-off value of ≤6. The sensitivity,specificity,Positive predictive value,Negative predictive value and accuracy of vaginal fluid creatinine to diagnose PROM were 99.89%,100.00%,100%,95.99% respectively with a cut-off value of >0.3

According to Ismail T. EL-Garhy et al (2019) [7] mean creatinine levels in vaginal fluid in group (I) & group (II) were.70 ± 0.88 and.04 ± 0.18 mIU/mL respectively. The difference was statistically significant (P value < 0.001). With creatinine cut-off value of 0.25 mIU/ml, the sensitivity & specificity in confirming PROM were 72 and 94% respectively.

These results cope with the study performed by Zanjani and Haghighil [8] who found that mean vaginal fluid creatinine levels in confirmed PROM group,suspected PROM group and control PROM group were 1.74 ± 0.8 mg/dl,0.45 ± 0.2 and 0.25 ± 0.1 mg/dl respectievely . The difference was statically significant (p<0.001) with sensitivity, specificity,positive predictivity and negative predictive values were 96.75%, 100%, 100%,and 96.8% respectievely and cut off value of 0.5mg/dl

In a recent study by Kuruoğlu [9] et al (2019), mean creatinine level in vaginal flushing fluid was 0.39±0. 31mg/dl in the PROM group, and 0.04±0.10mg/dl in the control group.

In present study vaginal fluid, creatinine was found to be a reliable marker for diagnosis of PROM Less time is required to diagnose PROM. Using vaginal fluid creatinine, which lead to timely obstetrics intervention minimizing the maternal and fetal risk.

In a study by Dr.Abhilash et al [10], mean AFI (cm)in women with PROM and control group were 5.18±1.96 and 9.58±2.43, respectively.AFI<6 was seen in 66% women with PROM and none of the control.

CONCLUSION

Vaginal fluid creatinine is the simple, practical, cost effective and easily accessible test and its incorporation in the low resource setting will be a game changer in the diagnosis of PROM. Further studies can be taken up with different gestational age groups for determination of cutoff values of vaginal fluid creatinine for diagnosing PROM.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 17-08-2021; **Accepted:** 07-09-2021; **Published:** 30-09-2021