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STUDY OF ROLE OF VAGINAL FLUID UREA & CREATININE IN DIAGNOSIS OF PREMATURE AND PRETERM PREMATURE RUPTURE OF MEMBRANES

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ABSTRACT

BACKGROUND:-Incidence of premature rupture of membranes (PROM) is 8% at term, in 60% of them labor begins spontaneously within 24 hours. The incidence of preterm premature rupture of membranes (PPROM) is 3% and 1/3 of preterm deliveries are attributable to PPROM. It is one of the significant causes of maternal and perinatal morbitity and mortality.

Conventional methods (Speculum examination of fluid leakage, Nitrazine test, fern test, USG) are associated with drawbacks. Other modalities like alfa feto protein, fetal fibronectin, HCG are not popular due to their high cost, availability and complexity.

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The fetal urine is one the main component of amniotic fluid during the second half of pregnancy, and this fact is utilized in measurement of urea and creatinine from the vaginal fluid for the diagnosis of PROM and PPROM. These tests are easy to carry out, as there is no need of extra equipments and reagents, and can be done routinely in low resource setting.

OBJECTVES:-To evaluate the reliability and to determine the cutoff values of vaginal fluid urea and creatinine in the diagnosis of PROM and PPROM.

MATERIALS AND METHODS:-This prospective case control study was performed on 200 women in the Department of Obstetrics &Gynaecology, JLN Medical College Ajmer Rajasthan. 100 pregnant women, who have complain of vaginal fluid leakage, PROM and PPROM was diagnosed via positive fluid leak,through sterile speculum examination and positive nitrazine paper test, were includedas study group and 100 pregnant women with negative speculum examination and negative nitrazine test with matched gestational agewere taken as control.

RESULTS :- Among cases mean value of creatinine was 1.46 $\pm$0.56 as compared to 0.09 $\pm$ 0.10 in controls. The mean value of urea in cases was 34.80 $\pm$ 13.37 as compared to 3.69 $\pm$ 1.6 in controls. There was significant difference in urea, creatinine values in both groups. According to ROC curve, the cut off point of creatinine was 0.48. Value > 0.48 showed 100% chance to develop PROM with 100% accuracy. According to ROC curve, the cut off point of urea value was 4.5. Value > 4.5 showed 100% chance to develop PROM with 100% accuracy.

CONCLUSION:- Present study showed that vaginal creatinine and urea values were highly significant to diagnose PROM. Cut off point of creatinine and urea > 0.48 and >4.5, respectively had 100% accuracy to diagnose PROM. Measurement of vaginal creatinine and urea value is rapid, cost effective, feasible, relevant and practical test specially in low resource settings.

Keywords- vaginal fluid urea & creatinine, diagnosis, premature rupture of membranes (PROM), preterm premature rupture of membranes (PPROM)

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INTRODUCTION:

The terms premature rupture of membranes (PROM) & preterm premature rupture of membranes (PPROM) are defined as rupture of membranes at or beyond 37 weeks of gestation and rupture of membranes before 37 weeks of gestation respectively.Incidence of PROM is 8% at term, in 60% of them labor begins spontaneously within 24 hours and in over 95% within 72 hours,however if immediate induction of labor is done, it leads to decreased maternal morbidity and neonatal ICU admissions, without increasing the rate of cesarean deliveries and operative vaginal deliveries.[1]

The incidence of PPROM is 3% and 1/3 of preterm deliveries are attributable to PPROM[2]. It is one of the significant causes of maternal and perinatal morbitity and mortality.Maternal effects include salpingitis, endometritisand sepsis[3]. Fetal complications include neonatal sepsis, fetal lung hypoplasia, chorioamnionitis,umbilical cord compression, etc[4,5].The pathophysiology leading to PROM has been shown to be different from the pathophysiology of PPROM.In PROM,at term generalised weakening of the membranes may result from physiological changes combined with shearing forces induced by contractions[6]. PPROM may result from a focal weakening rather than generalised weakness of the membranes.[7]PROM and PPROM can be diagnosed by taking proper history, clinical evaluation and doing some specific tests. Failure to diagnose such cases or over diagnosis i.e. false positive diagnosis of PROM and PPROM may lead to inappropriate management and hence leading to serious maternal and neonatal complications.

The conventional clinical diagnosis of PROM and PPROM are associated with many drawbacks, as history is reliable in 10% to 50% of cases only.Clinical examination and fern test have false negative results in 12% to 30% and 13% to 30% respectively, whereas false positive results of fern test is 5% to 30% cases.[9,10]Contamination by blood,urine or meconium may lead to false positive or negative results of Nitrazine test. Ultrasonic estimation of AFI is again not a reliable test to evaluate membrane rupture .[9, 10]Recently the focus has been shiftedon urea and creatinine levels of the cervico-vaginal discharge [11,12]. The fetus starts excretion of urine into amniotic fluid at 8th to 11th week of gestation. The fetal urine is one the main component of amniotic fluid during the second half of pregnancy, and this fact is utilized in measurement of urea and creatinine from the vaginal fluid for the

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diagnosis of PROM and PPROM. It is rapid, costeffective, feasible, relevant and practical test specially in low resource settings[13]. To evaluate the reliability and to determine the cutoff values of vaginal fluid urea and creatinine in the diagnosis of PROM and PPROM.

MATERIALS & METHODS:

This prospective case control study was performed on 200 women in the Department of Obstetrics &Gynaecology, JLN Medical College Ajmer Rajasthan, after approval of the local ethical committee and taking written informed consent from all pregnant women who participated in the study.

Table 1: Clinical diagnosis of PROM and PPROM[8]

Clinical diagnosis of PROM and PPROM is confirmed by 3
1 Observation of clear amniotic fluid flow or accumulation of fluid at posterior fornix with a sterile speculum.
2 Observation of change from yellow to blue colour of nitrazinepaper 3 Detection of palm leaf pattern in dried amniotic fluid with microscope (fern test).

Table 2 : Inclusion Criteria and Exclusion Criteria

INCLUSION CRITERIA:

1. Women with singleton live pregnancy between 20 - 34 years of age with gestational age of 28 to 42 weeks.
2. Women who are not a part of other studies.

EXCLUSION CRITERIA:

1. Pregnant women with vaginal spotting or bleeding.
2. Pregnant women with recent vaginal infection and having history of use of vaginal drugs.
3. Pregnant women with presence of regular uterine contractions in labor.
4. Pregnant women with known medical & prenatal complications.
5. Pregnant women with co-inhabitation in the prior night .
6. Pregnant women with fetal anomalies.

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All pregnant women who participated in study were subjected to full history taking, general and obstetric examination and sterile speculum examination to confirm leakage of amniotic fluid from the cervix.

100 pregnant women, who have complain of vaginal fluid leakage, PROM and PPROM was diagnosed via positive fluid leak, through sterile speculum examination and positive nitrazine paper test, were included as study group and 100 pregnant women with negative speculum examination and negative nitrazine test with matched gestational age were taken as control. All pregnant got USG abdomen for fetal viability. Thereafter vaginal washings from posterior vaginal fornix was taken for estimation of urea and creatinine from all the subjects of the study. 5 ml of sterile solution was injected into posterior vaginal fornix and 3 ml of it was withdrawn with the same syringe. Sample were send to Lab. Urea level was measured by enzymatic urease method and creatinine by chemical calorimetric method.

Statistical analysis of quantitative variables was performed in the form of mean and standard deviation (SD), and that of qualitative data was performed byindependent student's t test and chi square test. Sensitivity, specificity, positive predictive value(PPV), negative product value(NPV) were used for diagnostic accuracy. Receiver operating characteristics (ROC) curve analysis was used to establish an optimal cut off concentration. The result was evaluated with significance level of $p < 0.05$.

RESULT:

Among 100 cases and 100 controls, maximum patients (53 & 52) were in the age group of 19 -25 years. Mean age in study group was 25.36 years and 24.82 years in control group. There was no significant difference in age between both groups. There was equal participation of every religion in both groups. Maximum patients in both groups belonged to Hindu followed by Muslim and Sikhs. Mean Gestational age was also similar in both cases and controls. Mean gestational age of cases was 35.31 weeks and 35.14 weeks in controls. Among 100 cases, 35 were primigravida and 65 were multigravida and among 100 controls, 17 were primigravia and 83 were multigravida which was comparable.

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Table 3 : Correlation of Creatinine and Urea in Vaginal fluid

VARIABLES	CASE (100)		CONTROLS (100)		P value
	Mean	SD	Mean	SD	
Creatinine	1.46	0.56	0.09	0.10	<0.001
Urea	34.80	13.37	3.69	1.6	<0.001

Table 3 showed mean creatinine value was significantly higher in study group (1.46±0.56) in comparison to control group (0.09±0.10) [p <0.001]. Mean urea value was significantly higher in study group (34.80 ±13.37) in respect to control group (3.69±1.6) [p <0.001].

Table 4: Diagnostic accuracy

PARAMETER	Creatinine	Urea
Sensitivity	100%	100%
Specificity	100%	100%
Positive predictive value (PPV)	100%	100%
Negative predictive value (NPV)	100%	100%

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of creatinine and urea were 100%(Table 4). According to ROC curve, the cutoff point of creatinine was 0.48. Value >0.48 showed 100% chance to develop PROM with 100% accuracy. According to ROC curve, the cutoff point of urea value was 4.5. Value>4.5 showed 100% chance to develop PROM with 100% accuracy.

Correlation between gestational age and levels of creatinine was assessed using correlation coefficient r. The value of r was 0.0142. It was a positive correlation but the relationship between gestational age & levels of creatinine is weak, so there was no significant correlation between gestational age and levels of creatinine. Correlation between gestational age & urea levels was also assessed. The value of r was 0.0229 but again relationship was weak, so there was no significant correlation between gestational age and urea value.

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When the perinatal outcome was compared between 2 groups, it was poor in study group. In study group 12 % had full term cesarean deliveries, 7% had preterm cesareans and 29% had preterm vaginal deliveries as compared to 8%, 1% & 10 %,respectively in control group.

DISCUSSION:

In our study age, religion and obstetric score was found statistically insignificant, results were comparable to Pani SS et al [14] and Begam et al [8].In our study, mean creatinine value was significantly higher in study group (1.46± 0.56 in comparison to control group (0.09± 0.1)(p<.001) Begum et al showed mean creative value was significantly higher in study group (0. 67± 0.3) when compared to control group (0.16 ±0.09). Gada et al reported mean creatinine level was 0.64 in cases in comparison to control which was 0.14. Comparison was significantly higher.

In our study, mean urea level was significantly higher in study group (34.8± 13.37) than in control group (3.69±1.6)(p<.0001). Begum et al showed mean urea value was significantly higher in study group (12.6±4.8) when compared to control group (2.12± 1.31). Gada et al reported mean urea level was 29.67 in study group in comparison to controls which was 1.68. Comparison was significantly higher.Sabeeet al[16] found vaginal fluid urea &creatinine levels to be significantly higher in study group compared to control groups.

In our study, sensitivity, specificity, positive predictive value(PPV), negative predictive value(NPV) of creatinine and urea were 100% to confirm PROM with cutoff value of creatinine 0.48 and urea4.5. Osman et al 19 found sensitivity, specificity, PPV and NPV of creatinine and urea were 100% to confirm PROM with cutoff value of creatinine >0.41 and urea >0.23. Ghasemi et al 17 showed sensitivity, specificity,PPV and NPV of creatinine were 74.6%, 85%, 83% and 77.2%, respectively at cutoff point of 0.25. While sensitivity, specificity,PPV and NPV of urea were 79.7%, 82.5%, 81.8% and 80.4%, respectively at cutoff point 3.5. Diagnostic value of creatinine and urea was reported low by them for detecting PROM because of difference in the method of alboratory laboratory analysis and their cut off point. Gezer et at 18 found sensitivity, specificity, PPV and NPV of creatinine were 89%, 90%, 89.9% and 89%, respectively at cutoff point of> 0.12 to

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diagnose PROM. While sensitivity, specificity,PPV and NPV of urea was 88%,91%,90.7% and 88.3%, respectively at cutoff point of > 6.7.In our study, there was no significant correlation of gestational age with creatinine and urea level.

The limitation of this study was that it was applied to a certain population sharing a same geographical area, and hence a large study involving multiple centers can be done to reach to anfinal conclusion and determine an cutoff value for the determination of PROM and PPROM.

CONCLUSION:

Present study showed that vaginal creatinine and urea values were highly significant to diagnose PROM. Cut off point of creatinine and urea> 0.48 and >4.5,respectively had 100% accuracy to diagnose PROM. Measurement of vaginal creatinine and urea value is rapid, cost effective, feasible, relevant and practical test specially in low resource settings.

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