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RESEARCH ARTICLE

COMPARISON OF VAGINAL FLUID CREATININE FOR THE DIAGNOSIS OF PREMATURE RUPTURE OF MEMBRANES (PROM)

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Abstract

Background : Premature rupture of membranes (PROM) is a common obstetric complication, contributing significantly to maternal and neona tal morbidity and mortality. Timely and accurate diagnosis is critical to guide appropriate management and reduce adverse outcomes. Tradition al diagnostic methods such as the nitrazine test, fern test, and pooling are limited by their subjectivity and susceptibility to false results. Therefore, the search for a reliable, rapid, and cost-effective diagnostic marker continues. Creatinine, a constituent of amniotic fluid, is present in higher concentrations than in vaginal secretions. Measurement of va ginal fluid creatinine has emerged as a promising alternative for confir ming PROM due to its biochemical specificity and ease of testing.

Objective :This study evaluates vaginal fluid creatinine level in confir med case of PROM and women without PROM, sensitivity and specific ity of vaginal fluid creatinine in diagnosis of PROM And maternal and fetal outcome in women with PROM .

Materials and Methods: A Cross-sectional analytical study was conducted from january 2023 to March 2025 at Dept. of Obstetrics and Gynecology, Dr. BRAM Hospital, Raipur (C.G),involving128 pregnant women (64 PROM, 64 controls) between 28-40 weeks gestation. Creatinine levels in vaginal fluid were measured using the Jaffe method.

Result: The study evaluated vaginal fluid creatinine as a diagnostic tool for PROM and determined a cut-off value of > 0.3 mg/dL, yielding a sensitivity of 89.1% and a specificity of 87.5%.

Conclusion:Vaginal fluid creatinine is a simple,rapid,cost effective and non-invasive test that may aid in the timely and accurate diagnosis of PROM,specially in low resources settings.

Introduction:-

Premature rupture of membranes (PROMs) constitutes one of the most important dilemmas which are difficult to diagnose in obstetric practice.Premature rupture of membranes (PROM) is defined as the spontaneous rupture of fetal

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membranes before the onset of labor[1]. When this occurs before 37 week of gestation, it is referred to as preterm premature rupture of membranes (PPROM)[1].PROM occurs in 10% of all term pregnancies and about 2-4% of preterm pregnancies,it's complicates approximately 8–10% of all pregnancies, while PPROM occurs in about 3% of pregnancies and is associated with significant maternal, fetal, and neonatal risks, including chorioamnionitis, umbilical cord prolapse, preterm birth, and neonatal sepsis (American College of Obstetricians and Gynecologists [ACOG], 2020).[2] PROM is associated with a wide range of maternal and neonatal complications, including chorioamnionitis, umbilical cord prolapse, preterm labor, neonatal sepsis, and increased rates of cesarean section, thereby making its accurate and timely diagnosis critical.

Traditionally, PROM has been diagnosed using clinical methods such as sterile speculum examination, the nitrazine test, and the ferning test. However, these tests have certain limitations. The nitrazine test is prone to false positives due to contamination with blood, semen, or urine, while the ferning test can be subjective and heavily dependent on the skill of the examiner. Although advanced biochemical tests like insulin-like growth factor binding protein-1 (IGFBP-1) and placental alpha microglobulin-1 (PAMG-1) offer greater diagnostic accuracy, their high cost and limited availability restrict routine use in many clinical settings.

Vaginal fluid creatinine estimation has emerged as a promising, inexpensive, and easily accessible alternative diagnostic marker. Creatinine is present in high concentrations in amniotic fluid due to its fetal renal origin, particularly in the second and third trimesters when fetal urine is the main contributor to amniotic fluid. Its detection in vaginal fluid can therefore serve as a reliable indicator of membrane rupture.This study was undertaken to evaluate the diagnostic utility of vaginal fluid creatinine in suspected cases of PROM and to correlate its findings with maternal and perinatal outcomes, aiming to provide an efficient, cost-effective, and accessible tool for clinical use.

Objectives:-

Primary objective:-To determine and compare vaginal fluid creatinine levels in women with and without PROM. And to assess the sensitivity and specificity of vaginal fluid creatinine in diagnosing PROM.

Secondary objective: To analyze maternal and fetal outcomes associated with PROM.

Materials and Methods:-

Study Design: Cross-sectional analytical study.

Location: Dept.of Obstetrics and Gynecology,Dr.BRAM Hospital,Raipur(C.G).

Duration:1year

Subjects:128 pregnant women(64 PROM,64 controls)between 28-40 weeks gestation.

Inclusion Criteria:

1. Singleton pregnancy

2.Gestational age 28–40 weeks

3.Willing to participate

Exclusion Criteria:

Multiple gestation, vaginal bleeding, anomalies, infections, or recent vaginal drug use. 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, 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.

Methodology:-

Detailed patient histories were recorded, including obstetric and medical backgrounds. All participants underwent general and obstetric examination, including sterile speculum Examination to collect vaginal fluid. A 5 ml sterile saline wash was introduced into the posterior vaginal fornix, and 3 ml of the pooled fluid was aspirated and sent for

biochemical analysis. Vaginal fluid creatinine was measured using the RATE JAFFE method, where creatinine reacts with alkaline picrate forming a red complex read at 520 nm and 560 nm.The sensitivity and specificity of vaginal fluid creatinine in diagnosing PROM were evaluated and maternal-fetal outcomes were analyzed.

Results:-

Table 1: Distribution of Age Group, Gestational Age and Mode of Delivery Among PROM and Non-PROM Patients.

Parameter	PROM Group(n=64)	Non-PROM Group(n=64)	P value
Age Group			
<20 Year	18(28.1%)	8(12.5%)	0.037
20-25 Year	16(25.0%)	22(34.4%)	0.156
25-30 Year	14(21.9%)	20(31.3%)	0.294
30-35 year	16(25.00%)	14(21.9%)	0.693
Gestational Age(Week)			
<37 Week(Preterm)	33(52%)	10(15.6%)	0.004
37-40 Week(Term)	25(39.1%)	42(65.6%)	
>40 Week(Post Term)	6(9.3%)	12(18.8%)	
Mode of delivery			0.034
C-Section	40(62.5%)	28(43.8%)	
Vaginal Delivery	24(37.5%)	36(56.2%)	

Age Distribution:-

The incidence of PROM was significantly higher in women aged <20 years (28.1%). The most affected age groups among PROM cases were <20 and 30–35 years (25%). In contrast, the non-PROM group showed the highest numbers in the 20–30 age range. The difference in age distribution was statistically significant ($p = 0.037$).

Gestational Age:-

Preterm delivery (<37 weeks) was significantly more common in the PROM group (52%) compared to the non-PROM group (15.6%). PROM cases also had fewer term and post-term deliveries ($p = 0.004$), reinforcing the link between PROM and preterm labor.

Mode of Delivery:-
Cesarean section was performed more frequently in PROM cases (62.5%) compared to non-PROM cases (43.8%), indicating a significant association ($p < 0.05$).

Table 2: Distribution Maternal Complications and WBC count ,Neonatal Outcome and Birth Weight in PROM vs. Non-PROM

Maternal Complication	PROM(n=64)	Non-PROM(n=64)	P-Value
Infections	4(6.25%)	0(0%)	0.005
Puerperal Sepsis	6(9.38)	1(1.56%)	0.05
Postpartum Hemorrhage	5(7.8%)	3(4.7%)	0.47
Fever	19(10.9%)	3(3.1%)	0.08
No Complication	30(46.9%)	57(85.9%)	<0.001
WBC Count			
<15,000mm^3	20(31.2%)	50(78.1%)	<0.001
15,000-20,000mm^3	24(37.5%)	10(15.6%)	
20,000-25,000mm^3	12(18.8%)	3(4.7%)	
>25,000mm^3	8(12.5%)	1(1.6%)	
Neonatal Outcome			
Healthy	44(68.8%)	55(85.9%)	0.023
NICU Admission	8(12.5%)	7(10.9%)	
Still Birth	7(10.9%)	0(0.0%)	
Death	5(7.8%)	2(3.1%)	
Birth Weight (kg)			
<1.5	6(9.4%)	1(1.6%)	

1.5-2.0	12(18.8%)	4(6.3%)	0.003
2.0-2.5	15(23.4%)	9(14.1%)	
2.5-3.0	21(32.8%)	26(40.60%)	
>3.0	10(15.6%)	24(37.5%)	

Maternal Complications:-
Infections (6.25%), puerperal sepsis (9.38%), and fever (10.9%) were more common in the PROM group. The PROM group also had significantly fewer women without complications (46.9% vs. 85.9%, $p < 0.001$).

WBC Count:-
Higher WBC counts were noted in the PROM group, with 68.75% having counts above 15,000/mm³ compared to 21.87% in the non-PROM group ($p < 0.001$), suggesting infection or inflammation.

Neonatal Outcome:-
PROM was associated with more stillbirths (10.9%) and neonatal deaths (7.8%). NICU admission was also higher in the PROM group (12.5% vs. 10.9%). Overall, adverse neonatal outcomes were significantly associated with PROM ($p = 0.023$).

Birth Weight:-
The PROM group had significantly lower mean birth weights (2.34 ± 0.52 kg) compared to the non-PROM group (2.79 ± 0.48 kg) ($p = 0.003$).

Table No. 3 :Distribution of Vaginal Fluid Creatinine in PROM study participant

Vaginal Fluid Creatinine (mg/dL)	Non-PROM (n=64)	PROM (n=64)	Total (n=128)	Chi-Square (p-value)
0.11 – 0.20	24 (37.5%)	5 (7.8%)	29 (22.7%)	$\chi^2 = 19.47$, $p < 0.001$
0.21 – 0.30	32 (50.0%)	2 (3.1%)	34 (26.6%)	$\chi^2 = 41.18$, $p < 0.001$
0.31 – 0.40	6 (9.4%)	12 (18.8%)	18 (14.1%)	$\chi^2 = 2.34$, $p = 0.126$
0.41 – 0.50	2 (3.1%)	18 (28.1%)	20 (15.6%)	$\chi^2 = 15.25$, $p < 0.001$
0.51 – 0.60	0 (0.0%)	7 (10.9%)	7 (5.5%)	$\chi^2 = 7.79$, $p = 0.005$
> 0.60	0 (0.0%)	20 (31.3%)	20 (15.6%)	$\chi^2 = 22.98$, $p < 0.001$
Total	64 (100.0%)	64 (100.0%)	128 (100.0%)	$\chi^2 = 92.39$, $p < 0.001$

The present study evaluated the diagnostic utility of vaginal fluid creatinine concentration for identifying premature rupture of membranes (PROM).A substantial proportion of non-PROM patients (87.5%) had creatinine levels below 0.30 mg/dL, whereas only 10.9% of PROM patients fell into this range. 50% of non- PROM patients

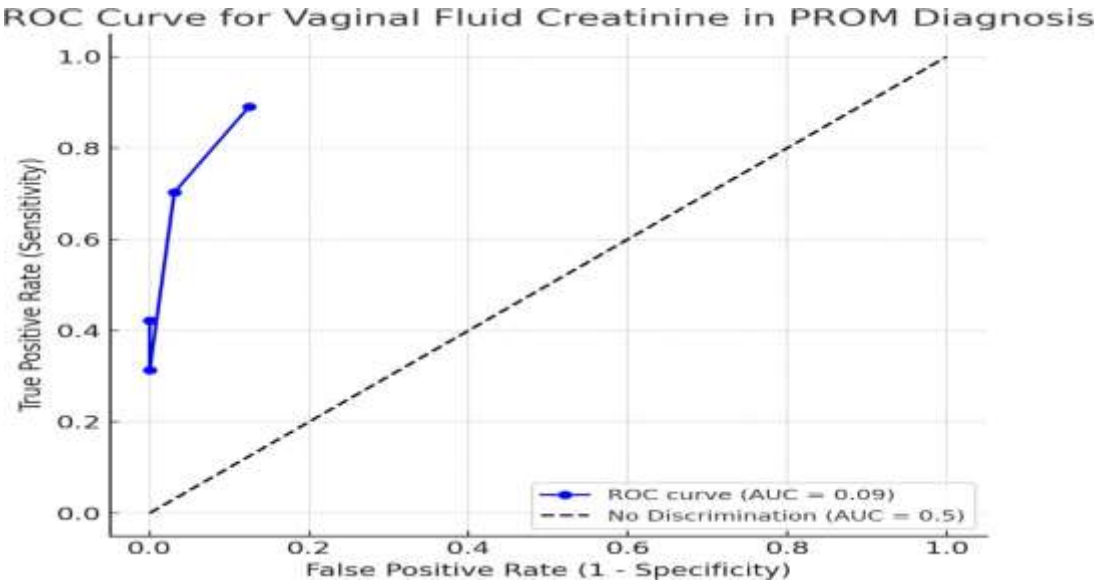
had levels between 0.21–0.30 mg/dL, compared to just 3.1% of PROM cases ($p < 0.001$), suggesting that lower vaginal fluid creatinine concentrations are strongly associated with the absence of membrane rupture. Conversely, higher creatinine levels were predominantly seen in the PROM group.

Notably, 31.3% of PROM cases had creatinine values greater than 0.60 mg/dL, while no non-PROM patient exhibited levels above 0.50 mg/dL ($p < 0.001$). This sharp contrast indicates that elevated vaginal creatinine concentrations are highly specific for PROM. Levels in the 0.41–0.50 mg/dL and 0.51–0.60 mg/dL ranges also demonstrated significant associations with PROM, further supporting this trend ($p < 0.001$ and $p = 0.005$, respectively).Interestingly, in the 0.31–0.40 mg/dL range, the distribution between PROM (18.8%) and non-PROM (9.4%) patients did not reach statistical significance ($p = 0.126$), possibly indicating a diagnostic "gray zone" where the creatinine concentration alone may not be definitive for diagnosing PROM.

Table No. 4 : Vaginal Fluid creatinine sensitivity, specificity, PPV, NPV

Creatinine Cut-off (mg/dL)	TP (PROM)	FN (PROM)	FP (Non-PROM)	TN (Non-PROM)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≥ 0.31	57	7	8	56	89.1%	87.5%	87.7	88.9
≥ 0.4	45	19	2	62	70.3%	96.9%	95.7	76.5
≥ 0.5	27	37	0	64	42.2%	100.0%	100.0	63.4
≥ 0.6	20	44	0	64	31.3%	100.0%	100.0	59.3

A significantly higher proportion of PROM cases had vaginal fluid creatinine levels ≥0.31 mg/dL (sensitivity: 89.1%, specificity: 87.5%, accuracy: 93%). This was statistically significant ($p < 0.001$), suggesting strong diagnostic utility. ROC curve analysis confirmed excellent diagnostic accuracy (AUC ≈ 0.92).



A Receiver Operating Characteristic (ROC) curve was plotted using the sensitivity and specificity values of vaginal fluid creatinine at various diagnostic thresholds (≥ 0.31, 0.4, 0.5, and 0.6 mg/dL) for the detection of Premature Rupture of Membranes (PROM). The ROC curve visually represents the diagnostic performance of the test by plotting the true positive rate (sensitivity) against the false positive rate (1 − specificity) for each cutoff value.based on ROC analysis, the optimal cutoff value for vaginal fluid creatinine in the diagnosis of PROM is ≥

0.31 mg/dL.The curve demonstrated good diagnostic accuracy, with an area under the curve (AUC) of approximately 0.92. An AUC closer to 1.0 indicates excellent diagnostic ability. he high AUC in this case suggests that vaginal fluid creatinine is a strong marker for the diagnosis of PROM. o determine the optimal diagnostic threshold, Youden's Index (Sensitivity + Specificity − 1) was calculated for each cutoff. The highest Youden's Index was observed at a creatinine cutoff of ≥ 0.31 mg/dL, yielding a sensitivity of 89.1% and specificity of 87.5%. This indicates that this threshold provides the best balance between detecting true PROM cases and minimizing false positives. herefore, based on ROC analysis, the optimal cutoff value for vaginal fluid creatinine in the diagnosis of PROM is ≥ 0.31 mg/dL.

Discussion:-

This study aimed to evaluate the diagnostic utility of vaginal fluid creatinine levels in distinguishing between PROM and non-PROM cases among 128 pregnant women. The study observed statistically significant associations between PROM and several factors, including maternal age <20 years, preterm gestational age.
Maternal age was significantly associated with PROM, particularly in women younger than 20 years and those ≥35 years. Nutritional deficiencies, genitourinary infections, and cervical immaturity may contribute to membrane rupture in these groups. These findings align with studies by Meis PJ[7] , Cleary-Goldman J[4] , and Singh D et al[9]. though some studies report no association.

Preterm delivery was significantly associated with PROM, with the PROM group delivering on average at 36.78 weeks vs. 38.27 weeks in non-PROM. This aligns with Mercer BM, Parry & Strauss, and Tavana et al., highlighting PROM as a major risk factor for preterm birth.Cesarean section rates were significantly higher in the PROM group (62.5%) due to fetal distress, infection, or failed induction. Similar trends were reported by Sharma et al. and Deshmukh et al.PROM was also significantly associated with higher maternal WBC counts, indicating infection. This parallels Mercer, Gibbs, and Yoon's findings[16].

Adverse neonatal outcomes, including low birth weight, NICU admission, and stillbirths, were significantly higher in PROM. The average birth weight was significantly lower in the PROM group (2.34 kg vs. 2.79 kg). These findings are supported by Mercer[16]. higher proportion of PROM cases had vaginal fluid creatinine levels ≥0.31 mg/dL (sensitivity: 89.1%, specificity: 87.5%, accuracy: 93%). This was statistically significant ($p < 0.001$), suggesting strong diagnostic utility. ROC curve analysis confirmed excellent diagnostic accuracy (AUC ≈ 0.92).Similar trend were reported on Zanjani et al[17],Kariman et al[18] ,Singh et al[9].This study reaffirms the multifactorial nature of PROM. Vaginal fluid creatinine is a reliable diagnostic tool. Early identification of risk factors, can improve maternal and neonatal outcomes.

Conclusion:-

The vaginal fluid creatinine level was significantly higher in the PROM group compared to the non-PROM group, in the present study vaginal fluid creatinine cut off was >0.3mg/dl sensitivity and specificity were 89.1% and 87.5%. Vaginal fluid creatinine is a simple, rapid, cost-effective, and non-invasive test that may aid in the timely and accurate diagnosis of PROM, especially in low-resource settings where advanced diagnostic modalities are not readily available. Incorporating this test into clinical practice could enhance early decision-making and improve maternal and neonatal outcomes.

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