

ROLE OF ALPHA FETO PROTIEN AS A MARKER IN DIAGNOSIS OF PREMATURE RUPTURE OF MEMBRANES IN RURAL POPULATIONPahula Verma¹, Sadhna Mathur², Gunjan³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: AIM: In India, especially in rural population multiple factors adversely affect the incidence of premature rupture of membrane. The purpose of this study is to test the amniotic fluid Alpha feto protein as a reliable marker for the detection of PPRM and to test its efficacy for the purpose in the rural India. **STUDY DESIGN:** This study was conducted in the Department of Obstetrics & Gynecology, NIMS Medical College & Hospital, Jaipur, Rajasthan. This was a cross sectional study during period of one year with sample size of 100 patients. **METHODS:** Patients who were at ≥ 24 weeks of gestation with the complains of leaking per vaginum. Sample for Alpha-fetoprotein (AFP) estimation was collected by instilling 5 ml of distilled water into vagina, irrespective of pooling of amniotic fluid and sent to the biochemistry lab for the analysis and for the estimation of alpha fetoprotein by using Electroluminescence enzyme immunoassay method. **RESULT:** The sensitivity, specificity, positive predictive value and negative predictive value are 92%, 98%, 92% and 98% respectively. **CONCLUSION:** The AFP can be used as reliable marker to avoid unnecessary obstretic interventions for diagnosis of PROM.

KEYWORDS: Alfa feto protein, Preterm rupture of membrane, Rural population.

INTRODUCTION: Premature rupture of membranes (PROM) is a syndrome characterized by rupture of the fetal membranes before labor. Preterm Prematurely Ruptured membranes (PPROM) defines as spontaneous rupture of the fetal membranes before 37 completed weeks and before labor onset¹. Prelabour rupture of membranes (PROM) is amniorrhexis in the absence of labour, irrespective of gestational age.² Approximately, 8–10% of term pregnancies will experience spontaneous PPRM prior to the onset of uterine activity.³ It complicates 2–4% of all singleton and 7–20% of twin pregnancies.^{4,5} Pathogenesis of preterm rupture is related to increased apoptosis of membranes cellular components and to increased level of specific proteases in the membranes and amniotic fluid. PPRM results from the activation of the collagen degradation, alteration in collagen assembly and cell death which lead to the weekend amnion.

Intra-amniotic infection and decidual hemorrhage (Placental abruption) occurring remote from term can contribute to the cause. The release of proteases into the choriodecidual tissues and amniotic fluid, leading to rupture of membranes. Placental abruption is seen in 4–12% of pregnancies complicated by PPRM, and is more common in pregnancies complicated by PPRM prior to 28weeks of gestation. Invasive uterine procedures performed during pregnancy (Such as amniocentesis, cordocentesis, chorionic villus sampling, fetoscopy, and cervical circlage) can damage the membranes, causing them to leak, but these are rare causes of PPRM.⁶ Rupture of the membranes typically presents as a large gush of clear vaginal fluid or as a steady trickle. The differential diagnosis includes leakage of urine (Urinary incontinence); excessive vaginal discharge, such as physiologic discharge or bacterial vaginosis, and cervical mucus (Show) as a sign of

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impending labor.⁷ Latency refers to the interval between rupture of the membranes and the onset of labor.

Maternal and fetal infection is the second major complication consecutive to PPRM, as chorioamnionitis complicates 10–36% of PPRM. Serious complications and mortality of neonates born prematurely due to PPRM is very high and inversely proportional to gestational age. Early and accurate diagnosis of PPRM would allow for gestational age-specific obstetric interventions designed to optimize perinatal outcome and minimize serious complications, such as cord prolapse and infectious morbidity (Chorioamnionitis, neonatal sepsis).⁸ Conversely, a false-positive diagnosis of PPRM may lead to unnecessary obstetric intervention, including hospitalization, administration of antibiotics and corticosteroids, and even induction of labor. Therefore, making an early and accurate diagnosis of PROM is important. Several markers have been studied, including α -fetoprotein (AFP), fetal fibronectin test (fFN), insulin-like growth factor binding protein-1 (IGFBP-1), prolactin, diamine oxidase activity, β -subunit of human chorionic gonadotropin (β -hCG) and placental α -microglobulin-1 in order to identify PROM^{9,10}. Estimation of AFP as a marker for prelabour rupture of membranes can be done by using techniques, like electroluminescence enzyme immunoassay.

AIM & OBJECTIVES: The purpose of this study is to test the amniotic fluid Alpha fetoprotein as a reliable marker for the detection of PPRM and to test its efficacy for the purpose in the rural India.

METHOD & MATERIAL: This study was conducted in department of Obstetrics and Gynaecology, NIMS medical college and hospital, Jaipur, Rajasthan. This study is done in the time period of March 2014 to March 2015. We have designed a cross-sectional study including 100 patients, who were at \geq 24 weeks of gestation with the complains of leaking per vaginum. All patients signed informed consent to use the clinical and ultrasound data for research purposes.

Antepartum haemorrhage and Intra-uterine death were exclusion criterias. A detailed past and family history was taken to rule out any systemic diseases. Complete general and systemic examination was done to rule out any pathology. A detailed per abdominal examination was done. Per speculum examination was performed for all the patients to note the presence of pooling of liquor. Sample for Alpha-foetoprotein (AFP) estimation was collected by instilling 5 ml of distilled water into vagina, irrespective of pooling of amniotic fluid and sent to the biochemistry lab for the analysis and for the estimation of alpha fetoprotein by using Electroluminescence enzyme immunoassay method. All other routine investigations with C-Reactive protein also sent.

An AFP level more than 30 ng/ml was taken as positive for prelabour rupture of membranes. Diagnosis of prelabour rupture of membranes was based on combined clinical diagnosis and laboratory criteria. Patients were divided into cases and controls. At least one clinical & two laboratory criteria's are essential for diagnosis. Clinical criteria were a frank leaking on per speculum examination, soaked pad or fever not attributable to any cause other than chorioamninitis. The laboratory criteria included increase in TLC, neutophilia in DLC and rise in C-reactive protein and ultrasound examination showing a decrease in AFI levels of less than 8. Efficacy of Alpha-foetoprotein was studied by using Chi-square test with p-value < 0.05 significant.

RESULTS: A total of 100 patients, the mean age of the cases is 24.86+/-6.8yrs, while it is 25.64+/-5.4yrs in controls. 62% (31/50) are primigravida in cases and 56% (26/50) in control, while 38% (19/50) and 44 % (22/50) are multigravida. 24% (12) patient came in early preterm gestation, 32%

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(16) in late preterm, while 44% (22) in term gestation in 50 cases. In control 28% (14), 24% (12), 48% (24) came in early, late preterm and term gestation respectively.

In our study, 2 (4%) and 3 (6%) patients suffering from hypertensive disorder of pregnancy in cases and control while 2 (4%) patients having twin pregnancy. Vaginitis /vaginal discharge is found as major predisposing factor for PROM as it seen in 15 (30%) and 30 (60%) patients in case and control group. 5 (10%) and 9 (18%) patients underwent in LSCS in previous pregnancy due to various reasons in case and control group respectively.

Incidence of twinning was also more common in patients with PROM i. e. 4% (2/50 patients) as compared to none in patients without PROM. The sensitivity, specificity, positive predictive value and negative predictive value are 92%, 98%, 92% and 98% respectively.

DEMOGRAPHIC DATA	CASES n=50 (%)	CONTROLS n=50 (%)
Mean age± standard deviation in (years)	24.86±6.8	25.64±5.4
Parity 1) Primigravida 2) Multigravida	31(62%) 19(38%)	28(56%) 22(44%)
Period of gestation in (weeks) 1) 24-31 weeks 2) 32-36 weeks 3) ≥37 weeks(term)	12(24%) 16(32%) 22(44%)	14(28%) 12(24%) 24(48%)

Table 1

Demographic characteristics n = 100.

DEMOGRAPHIC STUDY	CASES n = 50	CONTROLS n= 50
Hypertensive disorders of pregnancy	2(4%)	3(6%)
Twins	2(4%)	0(0%)
Vaginal discharge/ vaginitis	15(30%)	30(60%)
Previous LSCS	5(10%)	9(18%)

Table 2

Efficacy of alpha fetoprotein n =100.

ALPHA FETO-PROTEIN TEST	CASES n=50	CONTROL n=50	PREDICTIVE VALUE OF THE TEST
Positive	46(92%)	1(2%)	Positive predictive value- 92%
Negative	4(8%)	49(98%)	Negative predictive value-98%
	Sensitivity 92%	Specificity 98%	

Table 3

Risk factors in cases and controls n = 50.

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DISCUSSION: Given that PPRM is associated with the significant perinatal mortality and morbidity. The development of the correct test to confirm the diagnosis is of great benefit. The main aim of the present study was to know the role of the alpha fetoprotein in diagnosis of the premature rupture of the membranes. In our study, AFP was found to be a reliable test with a sensitivity of 92%, a specificity of 98%, a positive predictive value of 98.3%, a negative predictive value of 98%.

Levi et al; reported a sensitivity of 99%, a specificity of 91%, a positive predictive value of 95%, a negative predictive value of 99%. Their study results were better than those of the present study, because they used a kit which had a combination of AFP/PP12 monoclonal /polyclonal antibodies, for detection of PROM.¹¹ The present study's results were also compared to the study done by Ni CY et al; in this study, AFP had a 97.7% diagnostic sensitivity and 100% specificity. In this study result, there is high diagnostic sensitivity and specificity.

Because they have used the automated luminescence immunoassay system, the reporting time of the results was less than 1h.¹² Chhavi Rana Singh et al; in her study concluded that AFP is a reliable test with a sensitivity of 88.9%, a specificity of 98.5%, a positive predictive value of 98.3%, a negative predictive value of 90.1%.² Kishida T et al; reported that the incidence of overt preterm PROM was significantly higher in the patients with persistently detected AFP in preterm (3 in 4 cases) than in controls (3 in 21 controls).¹³ Shahin M et al; in his study showed vaginal fluid concentrations of the three marker were significantly higher in the PROM group than in the control group ($p < 0.001$).⁶ Receiver operator curve analysis indicated that AFP had 94% specificity, sensitivity, positive and negative predictive values.⁹

CONCLUSION: In this study it is proved that whenever there is difficulty in diagnosis of PROM, the AFP can be used as reliable marker to avoid unnecessary obstetric interventions.

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