

**COMPARATIVE STUDY BETWEEN PROLACTIN,
ALPHA-FETOPROTEIN AND B-SUBUNIT HUMAN
CHORIONIC GONADOTROPIN IN
CERVICOVAGINAL FLUID FOR DIAGNOSIS OF
PREMATURE RUPTURE OF MEMBRANE**

Thesis

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List of Abbreviations

ACOG	American College of Obstetricians and Gynecologists
AF	Amniotic fluid
AFI	Amniotic Fluid Index
AFP	Alpha feto protein
BPP	Biophysical profile
B-hCG	Beta-subunit human chorionic gonadotropin
DA	Dopamine
DAO	Diamine-oxidase
ELISA	Enzyme-Linked Immunosorbent Assay
FFN	Fetal fibronectin
GH	Growth hormone
HAFP	Human alpha-fetoprotein
IGFBPs	Insulin-like growth factor binding proteins
IGFs	Insulin-like growth factors
IUGR	Intrauterine growth retardation
LEEP	Loop electrosurgical excision procedure
LLETZ	Large-loop excision of the transformation zone
MIAC	Microbial invasion of the amniotic cavity '
MMPs	Matrix metalloproteinases
MSAFP	Maternal serum alpha-fetoprotein
MVP	Maximum Vertical Pocket
NST	Non-stress test
PBEF	Pre-B-cell colony enhancing factor
PL	Placenta lactogen
PPROM	Preterm premature rupture of membrane

PRL	Prolactin
PROM	Premature Rupture of Membrane
PTB	Preterm birth
PTL	Preterm labour
RDS	Respiratory distress syndrome
REM	Rapid-eye-movement
STD	Sexually transmitted diseases
VF_s	Vaginal fluids
VIP	Vasoactive intestinal peptide

INTRODUCTION

Premature rupture of membranes (PROM) is a condition which occurs in pregnancy when the amniotic sac ruptures before the onset of labor. Preterm prelabor rupture of membranes (PPROM) is a condition where the amniotic sac leaks fluid before 37 weeks of gestation (**Deering et al., 2007**).

Premature rupture of the membranes (PROM) is another most common problem in obstetrics, complicating approximately 5–10% of term pregnancies and up to 30% of preterm deliveries (**Scott, 2008**).

Intact fetal membranes with normal amniotic fluid are necessary for normal fetal growth and development. Membranes also serve as a barrier that separates the sterile fetal environment from the bacteria colonized in vagina. PPRM is the leading cause of the preterm birth and perinatal morbidity with tremendous socioeconomic impact in society (**Sadaf et al., 2011**).

Like many obstetric diseases, the etiology of PROM appears to be multifactorial; recently, subclinical intrauterine infection has been implicated as the major etiologic factor contributing to the pathogenesis of PROM.

Infection leads to recruitment of activated neutrophils and macrophages. These cells are capable of killing bacteria by

releasing reactive oxygen species (ROS) that destroy the bacterial cell wall. The primary ROS released hypochlorous acid, is also capable of damaging the fetal membrane directly and acts as a signal for the up-regulation of MMPs (*Mingione et al., 2006*).

Risk factors include a history of cervical insufficiency, antepartum bleeding, multiple gestations, previous PROM or preterm labor, tobacco use, cervical cerclage, and amniocentesis (*Waters and Mercer, 2009*).

The major cause of perinatal morbidity and mortality associated with PROM is prematurity . Morbidities related to prematurity include respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage, cerebral palsy, and sepsis. Other complications include in utero umbilical cord compression, cord prolapse and fetal distress, fetal malpresentation, placental abruption, chorioamnionitis with subsequent endometritis, and risk of operative delivery from this multitude of factors. Maternal sepsis is a rare but life-threatening complication reported in nearly 1% of cases (*El-Messidi and Cameron, 2010*).

Early and accurate diagnosis of ROM 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). Conversely, a false positive diagnosis of ROM may lead to unnecessary obstetric interventions, including hospitalization, administration of antibiotics and corticosteroids, and even induction of labor (*Shin Park et al., 2007*).

It is therefore important to achieve accurate diagnosis by identifying the presence of specific amniotic fluid markers in vaginal environment. These tests include measurement of vaginal pH, prolactin, α -fetoprotein, di-amine oxydase, insulin-like growth factor binding protein-1 (IGFBP-1), human chorionic gonadotropin and fetal fibronectin (*Esim et al., 2003*).

Esim et al (2003) and Kim et al (2005) demonstrated that the measurement of β -hCG may be a reliable, simple and rapid test for the diagnosis of PROM in the absence of vaginal bleeding because high levels of β -hCG in blood can interfere with the results of β -hCG levels in vaginal washing fluid.

Shahin and Raslan (2007) evaluated the clinical practicability of using AFP, β -hCG and prolactin in the diagnosis of PROM. Their statistical information clearly indicated that of the three markers, AFP was the best for diagnosing PROM.

Beesley et al (2008) found that qualitative and quantitative β -hCG assay of vaginal secretions are not useful for detecting ROM in term pregnancies.

All these tests have advantages and drawbacks. Up to now there is no gold standard test for PROM (***Kafali and Oksuzler, 2007***).

AIM OF THE WORK

This study was conducted to compare the reliability of the vaginal washing – fluid Prolactin, AFP and B-HCG assay and qualitative B-Human Chorionic Gonadotropin for the diagnosis of premature rupture of membranes (PROM) .

Chapter (1)

THE FETAL MEMBRANES

The membranous structure that surrounds the developing fetus and forms the amniotic cavity is derived from fetal tissue and is composed of two layers: the amnion (inner layer) and the chorion (outer layer).

The amnion is a translucent structure adjacent to the amniotic fluid, which provides necessary nutrients to the amnion cells. The chorion is a more opaque membrane that is attached to the decidua (the maternal tissue that lines the uterus during pregnancy). The amnion and the chorion are separated by the exocoelomic cavity until approximately three months gestation, when they become fused. Intact healthy fetal membrane is required for an optimal pregnancy outcome (**Steth Guller, 2011**).

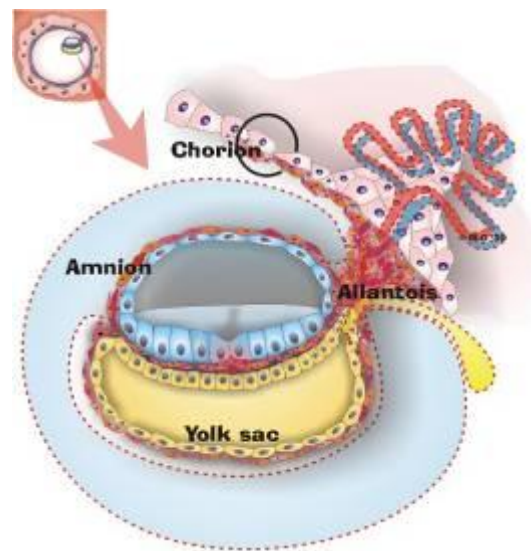
Inspection of the fetal membranes following delivery reveals amnion that is mildly adherent to the fetal side of the chorion. Small amounts of maternal decidual tissue can be observed attached to the outer, maternal side of the chorion (**Cunningham et al., 2005**).

Amnion and chorion fuse at about 12 weeks' gestation, via an intermediate layer of tissue, the spongy layer. The resulting amniochorion fuses intimately to the maternal decidua

parietalis at 20-25 weeks' gestation (*McParland and Taylor, 2005*).

The amnion and chorion laeve, although slightly adherent, are never intimately connected and usually can be separated easily, even at term (*Cunningham et al., 2005a*).

Anatomy of the amnion & chorion:



- | | |
|-----------------------|----------------|
| (1) Amnion | (2) Chorion |
| (3) Umbilical Vesicle | (4) Allantois. |

Fig (1): Fetal membranes: Anatomy (*Keith L. Moore 2007*).