Vaginal Fluid β-HCG for detecting Premature Rupture of Membranes

Thesis

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By

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Abstract

This is to evaluate the efficacy of detection of Human Chorionic Gonadotropin (β-HCG in vaginal fluid as a reference in cases complaining of premature rupture of membranes (PROM). Patients and methods: this study included 100 patients which where divided into 2 groups, study group (50 patients) and control group (50 patients). All patients were subjected to detailed history taking, general and local examination, ultrasonographic evaluation of amniotic fluid index (AFI) and speculum examination and sampling. Results: this study showed that β-HCG is a good reliable test in detecting cases of PROM Conclusion: The results showed that β-HCG is highly significant statistical test in detecting cases of PROM and it's more accurate and reliable than AFI in detecting the cases of PROM.

Key words: Human Chorionic Gonadotropin (β-HCG) – Vaginal Fluid – Premature Rupture Of Membranes.

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List of Abbreviations

AF	Amniotic fluid
AFI	Amniotic fluid index
AFP	Alpha-fetoprotein
AFS	Antenatal fetal surveillance
AFV	Amniotic fluid volume
AGA	Appropriate for gestational age
AROM	Artificial rupture of the membranes
BMI	Body mass index
BPP	Biophysical profile
CA	Chorioamnion
cAMP	Cyclic Adenosine Monophosphate
CBC	Complete blood count
cDNA	Complementary deoxyribonucleic acid
CIN	Cervical intraepithelial neoplasia
DAO	Diamino-oxidase
ECM	Extracellular matrix
EEC	Extra embryonic coelom
EM-O	Expectant management and induction with oxytocin
EM-P	Expectant management and induction with prostaglandin
FSH	Follicular stimulating hormone
GBS	Group-B streptococcus
HCG	Human chorionic gonadotropin
HIV-1	Human immunodeficiency virus type 1
HMD	Hyaline membrane disease
HOX A	Homeobox A
IAI	Intra-amniotic infection
IDDM	Insulin-dependent diabetes mellitus
IGF	Insulin-like growth factor
IGFBP-rPs	Insulin-like growth factor binding protein-related proteins
IGFBPs	Insulin-like growth factor binding proteins
IGFBP-1	Insulin-like growth factor binding protein-1
ILs	Interleukins
IUGR	Intra-uterine growth restriction
IVH	Intraventricular hemorrhage
IwO	Induction with oxytocin
IwP	Induction with prostaglandin
kDa	Killo Dalton

LEEP	Loop electrosurgical excision procedure
LH	Luteinizing hormone
LLETZ	Large-loop excision of the transformation zone
MIAC	Microbial invasion of the amniotic cavity
MMPs	Matrix metalloproteinases
MVP	Maximum vertical pocket
mRNA	Messenger ribonucleic acid
NEC	Necrotizing enterocolitis
NICHHD	National Institute of Child Health and Human Development
NICU	Neonatal intensive care unit
NIDDM	Non-insulin-dependent diabetes mellitus
NPV	Negative predictive value
NST	Non-stress test
P	Probability
PCOS	Polycystic ovary syndrome
PDA	Patent ductus arteriosus
PGE1	Prostaglandins E1
pIGFBP-1	Phosphorylated IGFBP-1
PPROM	Preterm premature rupture of membranes
PPV	Positive predictive value
PROM	Premature rupture of membranes
RDS	Respiratory distress syndrome
ROC curve	Receiver operating characteristic curve
ROM	Rupture of membranes
ROP	Retinopathy of prematurity
r-test	Correlation co-efficient test
SD	Standard deviation
SGA	Small for gestational age
SHBG	Sex hormone-binding globulin
SROM	Spontaneous rupture of membranes
STD	Sexually transmitted disease
t-test	Unpaired t-test
Term PROM	Term Prelabor Rupture of the Membranes
TIMPs	Tissue inhibitors of metalloproteinases
X^2	Chi-square test
Z	Mann Whitney Willcoxon test
2-DP	Two-diameter Pocket

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Introduction

The normal behavior of the fetal membranes is to maintain their integrity throughout pregnancy, and to rupture spontaneously in the later first stage or in the second stage of labour at term ***(McParland and Taylor, 2005).***

Spontaneous membrane rupture events can be separated into five distinct categories. The first, and most common, is natural rupture of the membrane (ROM) at term during labor. The second category is ROM at term but prior to the onset of labor, which is known as premature rupture of the membrane (PROM). The third category is iatrogenic membrane rupture caused by medical interventions either for diagnostic or therapeutic purposes, including amniocentesis or prenatal fetal surgery. The fourth category of ROM is intrauterine rupture of the amnion portion of the chorioamnion (CA) membrane during fetal development in the first three months of pregnancy. The fifth, and by far most significant, category of membrane failure is preterm premature rupture of the membrane (PPROM) ***(Calvin and Oyen, 2007).***

Spontaneous rupture of the amniotic membranes before the onset of labor occurs in about 8% of term pregnancies. Approximately 60% to 80% of women with prelabour rupture of membranes at term will enter spontaneous labour within 24 hours ***(Marowitz and Jordan, 2007).***

Failure to identify patients with membrane rupture can result in failure to implement obstetric measures. Conversely, the false diagnosis of membrane rupture can lead to inappropriate interventions such as hospitalization or induction of labour. Therefore, any biological test used to establish a correct diagnosis must be reliable, simple and rapid ***(Esim et al., 2003).***

Phelan and colleagues (1987) described the clinical utility of quantification using the amniotic fluid index. This is calculated by adding the vertical depths of the largest pocket in each of four equal uterine quadrants.

The absence of a noninvasive "gold standard" test for the diagnosis of membrane rupture has led to the search for alternative biochemical markers; vaginal prolactin, α-fetoprotein, fetal fibronectin *etc.* have previously been studied ***(Sucak et al., 2005).***

Human chorionic gonadotropin is a glycoprotein produced exclusively by syncitio-trophoblasts in the placenta. As pregnancy progress, mean level of (β-hCG in maternal circulation increase to approximately 54,000 mIU/mL at 8-12 weeks of gestation. It then declines rapidly reaching a nadir at approximately 20 weeks of gestation; this nadir is maintained at approximately 12,000 mIU/mL during the third trimester. **β-hCG** is present in AF as well as maternal blood and urine, at concentrations ranging from approximately 2000 to 70,000 mIU/mL **(Kletzky *et al*., 2004).**

Because HCG is secreted by cervical glands; a certain level should be present in vaginal fluid. Therefore, HCG levels will be measured and compared in the vaginal fluid of normal pregnant women and pregnant women with PROM. It is will be hypothesized further that levels of hCG in vaginal fluid would be a good diagnostic indicator of PROM , if these values were low compared with those in AF **(*Esim et al., 2003).***

Aim of the Work

This study is a case-control study aimed; (1) to evaluate the diagnostic potential of human chorionic gonadotropins (β-HCG) measurement in vaginal fluids as an indicator of ruptured fetal membranes (ROM), (2) to compare the efficacy of (β-HCG) measurement and amniotic fluid index (AFI) assessment in the diagnosis of ROM.

Chapter (1)

Anatomical Considerations of Fetal Membranes

The membranes surrounding the amniotic cavity are composed of the amnion and the chorion, which are closely adherent layers consisting of several cell types, including epithelial cells, mesenchymal cells, and trophoblast cells, embedded in a collagenous matrix ***(Parry and Strauss., 1998).***

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 ***(McFarland 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, 2005).***

AMNION

It is the innermost fetal membrane and is contiguous with amniotic fluid. The amnion is the tissue that provides almost all of the tensile strength of the fetal membranes. Therefore, the development of the components of the amnion that protect against its rupture or tearing is vitally important to successful pregnancy outcome ***(Cunningham, 2005).***

Development of the amnion:

The amnion develops from an ectodermal cell nest in the dorsal aspect of the embryo 8 days after conception ***(Calvin and Oyen, 2007).***

When first formed the amnion is in contact with the body of the embryo, but about the fourth or fifth week fluid (liquor amnii) begins to accumulate within it. This fluid increases in quantity and causes the

amnion to expand and ultimately to adhere to the inner surface of the chorion, so that the extra-embryonic part of the celoam is obliterated ***(Benirschke and Kaufmann. 2000).***

The amniotic sac obliterates the space between it and the chorion by 10–12 weeks of gestation and by 16 weeks the chorioamnion has pushed up against the decidua of the uterine wall ***(Calvin and Oyen, 2007).***

Small cells that lined inner surface of trophoblasts have been called amniogenic cells, the precursors of amniotic epithelium ***(Cunningham, 2005).***

Structure of the amnion:

The human amnion is composed of five distinct layers **(Fig. 1)** ***(Parry and Strauss, 1998).***

(1) The epithelium:

The innermost layer, nearest the fetus, is the amniotic epithelium. It has been shown that there is rapid mitotic division of the amniotic epithelium in early pregnancy, but this decreases by the 6^{th} month and reaches low values thereafter ***(Parry and Strauss, 1998).***

The apical surface of the epithelial cells is replete with highly developed microvilli, consistent with a major site of transfer between amniotic fluid and amnion ***(Cunningham, 2005).***

The amniotic cavity expands most rapidly in the last trimester, and the epithelial cells must replicate or hypertrophy at a rate sufficient to maintain this continuous epithelium ***(Bryant-Greenwood and Millar, 2000).***

(2) The basement membrane:

Amniotic epithelial cells secrete collagen types III and IV and non-collagenous glycoproteins (laminin, nidogen, and fibronectin) that form the basement membrane, the next layer of the amnion ***(Parry and Strauss, 1998).***