Placental Alpha 1 Micro Globulin Detection in Cervico-vaginal Secretions In The Diagnosis Of Preterm Premature Rupture of The Membranes

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by

Medhat Mounir Kamel

Research fellow, National Research Center

(M.B.B.CH)

Supervisors

Dr. Mouhamed Roshdy Mahmoud

Professor of Obstetrics and Gynecology

Faculty of Medicine-Cairo University

Dr. Foad Abd El Kader Abo Hamela

Assistant Professor of Obstetrics and Gynecology

Faculty of Medicine-Cairo University

Dr. Mariem Mahmoud Mouhamed

Lecturer of Obstetrics and Gynecology

Faculty of Medicine-Cairo University

FACULTY OF MEDICINE

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بِسْمِ اللّهِ الرَّحْمنِ الرَّحِيمِ

"وَأَنزَلَ اللّهُ عَلَيْكَ الْكِتَابَ
وَالْحِكْمَةَ وَعَلَمَكَ مَا لَمْ تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ اللّهِ عَلَيْكَ عَظِيمًا"

صدق الله العظيم

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Abstract

Premature rupture of membranes (PROM) is the rupture of fetal membranes at least 24h before onset of labour ,while preterm premature rupture of membranes (PPROM) is the rupture of fetal membranes which proceed the onset of labour for more than 24hours before 37 weeks of gestation**.** Correct diagnosis of PROM has great importance because failure of diagnosis can lead to unwanted obstetric complications. The false diagnosis of membrane rupture can lead to inappropriate interventions such as hospitalization or induction of labor. Therefore, many diagnostic test has been discovered including many biochemical markers as B-HCG, urea , creatinine , thyroid hormones fetal fibronectin and ILGF-1 but non of them proved to be the golden standard in diagnosis of (PROM). Any biochemical test used to establish a correct diagnosis must be reliable, simple and rapid**.** ***PAMG-1*** detection in cervicovaginal discharge is a new diagnostic test for ROM .it can be used as a marker for diagnosis due to its unique characteristics (i.e., high concentration in the amniotic fluid, low level in blood , and extremely low background level in cervicovaginal secretions with intact fetal membranes)**.** ***Amnisure*** is the test used for detection of PAMG-1 in cervicovaginal discharge. In this study the result of Amnisure test was compared to other diagnostic test as Ferning, Nitrazine ,pooling and AFI. This prospective case-control study was carried out at Cairo University Hospital. The study included 60 pregnant women between 20-37 weeks of gestation were subdivided into two groups of women. These result proved that the use of Amnisure test is better than other traditionally available technique for diagnosis of PROM. So its our recommendation is to use Amnisure test for diagnosis of PROM, although the cost of the test is high in comparison to other diagnostic test but the high accuracy and reliability of it is a great benefit.

Keywords:

Placental alpha$_1$microglobulin

Cervicovaginal

Amnisure

Premature rupture of membranes

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Introduction

Membrane rupture is one of the most common disorders during pregnancy, it may occur at any time in the pregnancy. It may happen appropriately with the onset of labor at term, or prematurely, prior to the onset of labor. When occurring prior to the onset of labor for more than 24 hours at term this is referred to as premature rupture of membranes or PROM. Alternatively, it may occur in a preterm gestation, less than 37 weeks. This is referred to as preterm premature rupture of membranes or PPROM ***(Deering S., et al., 2007)***.. Regardless of when membrane rupture takes place, the method of diagnosis is the same.

PROM occurs in approximately 10% of all pregnancies after 37 weeks gestation and in 2-3.5% of pregnancies before 37 weeks gestation ***(Simhan H., et al.,2005)***.

PROM constitutes a major etiological factor of prenatal and postnatal complications. It is a significant cause of premature delivery and other maternal and neonatal complications ***(Simhan H., et al.,2005)*** .

The management of a patient with PROM and PPROM is expensive and difficult as the clinician attempts to balance the risk of prolonging pregnancy against the risks of acquiring intrauterine and maternal infection and the immaturity of lung development. Therefore, correct and timely diagnosis of this disorder is critical. ***(Hofmeyrv G.,2009).***

Symptom of membrane rupture (either PROM and PPROM) can be conducted when the following symptoms/conditions occur: Vaginal secretions increase or become watery, especially in women at the risk of preterm delivery or after an insult to the abdomen, as a fall, strike, or shake of the stomach, leading to potential rupture of fetal membranes visible or unnoticed leakage of amniotic fluid. .

Evaluation of the patient begins with full history taken , full general and local examination, then a sterile speculum examination is done from which three signs of membrane rupture are sought, including: Pooling, Positive Ferning test ,and Positive nitrazine test.

Additionally, oligohydramnios (low amniotic fluid level) may be detected by sonographic examination suggestive of amniotic fluid loss secondary to membrane rupture but not conclusive.

In diagnosing PROM, the history and physical examination alone often are inadequate to confirm the status of the membranes. Fluid may not be present in the vagina for evaluation, the fluid may be contaminated with urine, cervical mucus, vaginal discharge, blood, or meconium. Because of these difficulties, multiple cytological, biochemical, colorimetric and sonographic methods have been developed for detection of ruptured membranes. Despite significant advances in technology, no one test has been found to be completely accurate, and the diagnosis still requires an integration of historic factors, physical examination, and laboratory testing.

Noting that pooling strongly supports the diagnosis of rupture of membranes (ROM). However this finding is not always present in a patient with ROM.

The method of “ferning” has been associated with false positive results described secondary to contamination with fingerprints on a slide or contamination with semen and cervical mucus. ***(ACOG., 2007)***. False negatives (5%-10%) may be caused by dry swabs or contamination with blood. The strength of the fern test to differentiate between amniotic and nonamniotic fluid in vaginal discharge was investigated in the

laboring and nonlaboring patient with noted differences in sensitivity and specificity. Sensitivity and specificity in the laboring group were 98.0% and 88.0%. In the nonlaboring group, sensitivity and specificity were only 51.4% and 70.8%, respectively ***(ACOG.,2007).***

The Nitrazine evaluation is associated with false positive results ranging from 1% to 17% that can result from alkaline urine, blood, semen, vaginal discharge in cases of bacterial vaginosis, or Trichomonas infection. Sensitivity and specificity have been reported at 90.7% and 77.2% respectively***(Cousins L.,et al 2005).***

Membrane rupture is suspected to have occurred if any of the above three findings are present and diagnosis is confirmed when all three findings are noted. However, all three findings are not mandatory for the diagnosis of membrane rupture. When two of three are present, clinical correlation is exercised. Frequently, equivocal results are obtained when diagnostic criteria are not met and result in false positive and false negative diagnosis of ruptured membranes.

There are many biochemical tests developed to diagnose ROM .Any biochemical test used to establish a correct diagnosis must be reliable, simple and rapid ***(Esim E., et al., 2002)***. These biochemical markers like vaginal diaminoxidase, prolaction, alpha-feto-protein (AFP), fetal fibronectin, and insulin-like growth factor binding protein-1 (IGFBP-1) have been studied ***(Lockwood et al.,1994)***. however, prolactin and AFP were not useful markers for PROM because of the overlap in concentrations between pregnant women with and without ruptured membranes ***(Gaucheand P., et al.,1997)***. Moreover, chorionic release of

fetal fibronectin preceding delivery in patients with intact membranes may also lead to false-positive results. IGFBP-1 is a major protein of amniotic fluid. The dipstick method can detect IGFBP-1 in 5 minutes ***(Erdemoglu E. and Mongan T., 2004)***.

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Non of these marker is considered to be a gold standard test for diagnosis of PROM due to low sensitivity, and specificity and difficult technique of sample collection.

When the diagnosis remains unclear, an invasive method may be applied where amniocentesis is done and a dye (Evans Blue or Fluorescein) is injected and leakage from the cervix is visualized ,this method is highly invasive and has many complications and can itself induce a PROM.

In this study we test the value of detection of placental alpha one microglobulin (PAMG-1) in cervicovaginal discharge as a diagnostic test for ROM.

Aim of the Work

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The aim of this work is to evaluate the value of detection of PAMG-1 in cervicovaginal discharge in diagnosis of premature rupture of membranes .in comparison to the other traditionally available methods such as Nitrazine , Ferning ,pooling and ultrasound.