

Role of Vaginal fluid creatinine in diagnosing women of rupture of fetal membranes

Thesis

Submitted for the Partial Fulfillment of Master Degree in
Obstetrics and Gynecology

By

Tahir Ahmed Tahir Abu laban

M.B.B.CH, Ain Shams University (2013)

Visitor Resident of Ob/Gyn. at Ain Shams University Maternity Hospital.

Under Supervision of:

Dr. Abd el Megeed Ismail Abd el Megeed

Professor of Obstetrics and Gynecology
Faculty of Medicine Ain Shams University

Dr. Ahmed Mahmoud Hussein

Lecturer of Obstetrics and Gynecology
Faculty of Medicine Ain Shams University

Dr. Emad Maarouf Abdelatif

Lecturer of Obstetrics and Gynecology
Faculty of Medicine Ain Shams University
Faculty of Medicine
Ain Shams University

2018

Acknowledgement

First and foremost, praise and thanks must be to Allah, who guides me throughout life.

I would like to express my deepest gratitude and thanks to Prof. Dr. Abd el megeed Ismail, Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for his kind support, continuous encouragement and great help throughout the work. It was a great honor to be a student working under his supervision.

I can't forget to thank Dr., Ahmed Hussein, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his careful supervision and continuous advices and cooperation.

Last but not least, I can't forget to thank all members of my Family, specially my Parents for their kind care and support.

Also I would like to thank all pregnant ladies who accepted to be a part of this study.

✍ Tahir abu Saban

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TABLE OF ABBREVIATION

+ve	positive
ACTH	Adreno Cortico Trophic Hormone
AF	Amniotic fluid
AFI	Amniotic fluid index
AFP	Alfa-feto protein
B M I	Body Mass Index
BV	Bacterial Vaginosis
CBC	Complete Blood Count
CRH	Corticotropin releasing hormone
CRP	C-Reactive Protein
CS	Caesarian Section
CT	Chlamydia Trachomatis
DAO	Diamine Oxidase
DHEA-S	Dehydropaindrosterone sulfate
EDS	Ehlers danlos syndrome
ELISA	Enzyme-Linked Immuno Sorbant Assay
ESR	Erythrocyte Sedimentation Rate
fFN	Fetal Fibronectin
FHR	Fetal Heart Rate
GA	Gestational Age
GBS	Group B Streptococci
HCG	Human Chorionic Gonadotropin
IGFBP-1	Insulin-like Growth Factor Binding Protein-1
IUGR	Intra Uterine Growth Restriction
IVH	Intraventricular hemorrhage
MMP	Matrix metalloproteinases
NICU	Neonatal Intensive Care Unit
NPV	Negative predictive value
NS	Non Significant
PG	Prostaglandin
PGE1	Prostaglandin E1
PGE2	Prostaglandin E2
PGF2	Prostaglandin F2

Index

PPROM	Preterm premature rupture of membrane
PPV	Positive predictive value
PROM	Premature rupture of membrane
PTL	Preterm Labour
RDS	Respiratory Distress Syndrome
ROM	Rupture of membrane
ROS	Reactive oxygen species
S/D	Systolic /Diastolic
SD	Standard Deviation
SPSS	Statistical Package for Science and Society
TIMP	Tissue inhibitors of metalloproteinases
TLC	Total Leukocytic Count
-ve	Negative
WBCs	White Blood Cells

Introduction

Preterm delivery is a worldwide public health problem, and it occurs in approximately 6–12% of all pregnancies. (*Chang et al., 2013*)

Premature rupture of membranes (PROM), or pre-labor rupture of membranes, is a condition that can occur in pregnancy. It is defined as rupture of membranes (breakage of the amniotic sac), commonly called breaking of the mother's water(s), more than 1 hour before the onset of labor. (*Practice Bulletins, 2013*).

If rupture occurs before 37 weeks, called preterm premature rupture of membranes (PPROM), the fetus and mother are at greater risk for complications. PPRM causes one-third of all preterm births, and babies born preterm (before 37 weeks) can suffer from the complications of prematurity such as respiratory distress, brain bleeds, infection, necrotizing enterocolitis (death of the fetal bowels), brain injury, muscle dysfunction, and death. (*Mackeen, 2014*)

Prematurity from any cause leads to 75% of perinatal mortality and about 50% of all long-term morbidity. (*Hösli*

and Irene ,2014). PROM is responsible for 20% of all fetal deaths between 24 and 34 weeks gestation. **(Cunningham,2014)**

PPROM can also lead to chorioamnionitis (an infection of the fetal membranes and amniotic fluid) which can be life-threatening to both the mother and fetus. Women with PPRM will develop an intramniotic infection 15-25% of the time. **(Beckmann and Charles ,2010)**

PPROM is usually clinically diagnosed by a history of watery vaginal discharge and confirmed on sterile speculum examination. Diagnosis of PPRM relies on the clinician's ability to document three clinical signs i) visual pooling of clear fluid in the posterior fornix of the vagina or leakage of fluid from the cervical os; ii) an alkaline PH of the cervicovaginal discharge demonstrated by the yellow nitrazine paper turning blue (nitrazine test); iii) microscopic ferning of the cervicovaginal discharge on drying. **(ACOG Committee on Practice Bulletins, 2007)**

Conventionally tests such as the nitrazine tests and ferning tests have been used to diagnose PPRM. The fern

test refers to microscopic crystallization of amniotic fluid on drying and may give false positive results due to finger prints or contamination with semen and cervical mucus and false negative results due to technical error or contamination with blood. **(Rosemond et al., 1990)**

Reported sensitivity and specificity for the fern test are 51% and 70% respectively in patients without labor and 98% and 88% respectively in patients with labor. **(Smith, 1976)**

These tests become progressively less accurate when more than one hour has elapsed after membrane rupture. Nitrazine test is associated with high false positive rates when cervicitis, vaginitis (bacterial vaginosis) and contamination with blood urine, semen and/or antiseptic agents. **(Matthew et al., 2014)**

Early and accurate diagnosis of PPRM would allow for gestational age specific obstetric interventions designed to minimize serious complications and optimize perinatal outcomes. Conversely a false positive diagnosis of PPRM may lead to unnecessary obstetric interventions including hospitalization, administration of antibiotic, corticosteroids

and potentially induction of labor. (*Hannah et al., 2000*)
(*Healy et al., 2004*)

Timely and accurate diagnosis of PPRM is critical to optimize pregnancy outcomes, so critical that amniodye test may be recommended if conventional tests for PPRM are equivocal and pregnancy is remote from term. This test involves amniocentesis and installation of dye (indigo carmine) into the amniotic cavity. Leakage of blue stained fluid into the vagina within 20 -30 minutes as evidenced by staining of tampon is regarded as definitive diagnosis of PPRM. Although considered by many investigators as the gold standard test the amniodye test is an invasive procedure. (*Aaron et al., 2008*)

Recently some new non-invasive tests are used in, based on the detection of specific proteins found in amniotic fluid. There are a number of rapid immunoassay tests commercially available, of which the most commonly used in The United States are Actim® PROM, designed to detect insulin-like growth factor binding protein-1 (IGFBP-1) and Amnisure® which detects the presence of placental alpha Macroglobulin-1 (PAMG-1), but these tests are expensive. (*Montse Palacio et al., 2014*)

Creatinine is a break-down product of creatinine phosphate in muscles and is usually produced at a fairly constant rate and is mainly filtered out of the blood by kidneys (*Delanghe et al., 1989*)

Creatinine of fetal urine is the most important source of amniotic fluid in second half of pregnancy (*Kafali and Oksuzla, 2007*)

Recently the focus has been on urea and creatinine in cervicovaginal discharge. Studies reported the accuracy of urea and creatinine to determine the PROM from 90-100% (*Kafali and Oksuzla et al., 2007*)

Aim of the Study

Research Hypothesis:

In pregnant women with preterm premature rupture of membranes vaginal fluid creatinine could be accurate in making diagnosis.

Research Question:

Is vaginal fluid creatinine measurement accurate in diagnosing premature rupture of membranes?

Aim:

This study aims to assess the accuracy of vaginal fluid creatinine measurement in diagnosing premature rupture of membranes.

Chapter 1

The Fetal Membranes

Fetal Membranes:

Chorioamnion, the membranes surrounding a fetus during gestation (*Michelle et al., 2005*).

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*).

Anatomy of the amnion & chorion:

(1) Amnion

(2) Chorion

(3) Fetal Fibronectin

(4) Decidua

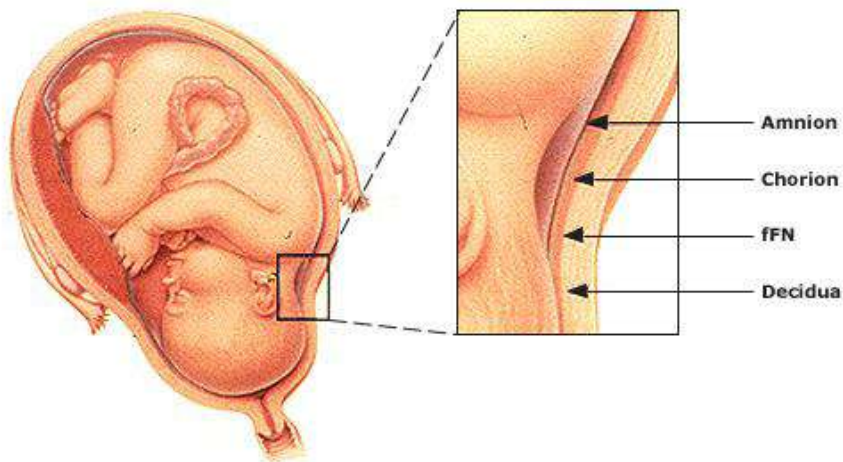


Figure 3 Fetal membranes: Anatomy (Seth Guller, 2006).

Anatomy of the amnion:

Amnion is a thin translucent membrane. The fetal Surface of which is smooth and glistening. It is reflected from the root of the cord to the fetal surface of the placenta, and then at the margin of the placenta it is continuous to line the surface of the chorion leave. Through the amnion three umbilical vessels can be seen imbedded in Wharton jelly, these are two umbilical arteries and one umbilical vein. The amnion is loosely attached to Wharton jelly except at the site of insertion of the umbilical cord in the placenta where they are firmly attached (*Mcparland and Bell, 2004*). It is divided into 3 parts (*Sagol et al., 2001*):

- A- Placental amnion: covers the inner aspect of the placenta.
- B- Dependent amnion: 1-2 cm overlying the internal os of the cervix.
- C- Reflected amnion: the reminder part of the amnion.

Anatomy of the chorion:

The chorion is the specialized outer fetal envelope that is adjacent to the outer aspect of the amnion and through which the major branching umbilical vessels travel on the surface of placenta (*Novak,1991*).