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β-HUMAN CHORIONIC GONADOTROPIN ASSAY IN VAGINAL WASHING FLUID FOR THE ACCURATE DIAGNOSIS OF PREMATURE RUPTURE OF MEMBRANES

Thesis

Submitted for Partial Fulfillment of Master Degree in Obstetrics and Gynecology

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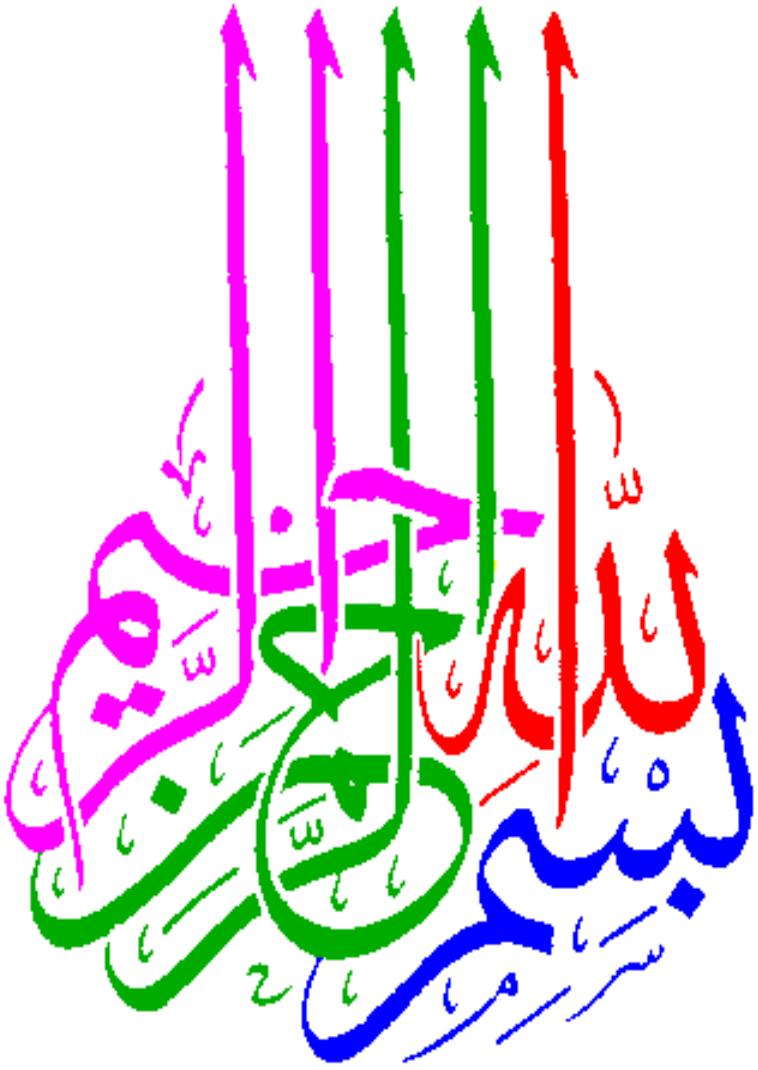
2017


بسم الله الرحمن الرحيم

Acknowledgements

First, thanks to Allah, for all the countless gifts I have been offered. I would like to express my deepest thanks, gratitude and appreciation to our *Prof. Dr. Mohamed Nabegh Elmahalawi,* professor of Obstetrics and Gynecology, Ain Shams University, to whom I am greatly indebted and deeply grateful for his constant supervision and encouragement together with his valuable suggestions. He gave me much of his unlimited experience in scientific research, which helped me to perform this work.

I am really grateful and indebted to *Prof. Dr. Mostafa Ibrahim Ibrahim*, professor of Obstetrics and Gynecology; Faculty of Medicine, Ain shams University, for his kind supervision, support and for advising me.

I'm very grateful to *Dr. Radwa Mansour Mohamed*, Lecturer in Obstetrics and Gynecology, Faculty of Medicine, Ain shams University, for her support and guidance.

Many thanks to the patients who agreed to be involved in this study, without whom; no medical research could be done.

To my Parents, My Husband and my Kid

Contents

	Page
Protocol ……	*V-XXI*
Introduction……	1
Aim of the work……	4
Review of literature:	
• The fetal membranes & the amniotic fluid……..	7
• Mechnism and mangment of PROM ……	20
Patients and Methods……	57
Results……...	65
Discussion……..	73
Summary……..	82
Conclusion&recommendation……	85
References…….	87
Arabic Summary……..	108

List of Abbreviations:

A.F.	Amniotic Fluid
AFI	Amniotic Fluid Index
AFV	Amniotic Fluid Volume
CNS	Central Nervous System
DAO	Vaginal diamine-oxidase
fFN	Fetal Fibronectin
GBS	Group B Streptococcus
IGFBP-1	Insulin-Like Growth Factor Binding Protein-1
IGFs	Insulin-Like Growth Factors
LEEP	Loop Electrosurgical Excision Procedure
MMPs	Matrix Metalloproteinases
MV	The Maximum Vertical Pocket
PAMG- 1	Placental Alpha Microglobulin-1
PBEF	Pre-B-Cell Colony Enhancing Factor
PPROM	Preterm Prelabor Rupture of Membranes
PROM	Prelabor Rupture of Membranes
RDS	Respiratory Distress Syndrome
ROC	Receiver-operating characteristic
TIMP	Tissue Inhibitors of Matrix Metalloproteinases
TNF-α	Tumor Necrosis Factor-Alpha
β-hCG	Beta Subunit Of Human Chorionic Gonadotropin

List of tables:

Tab.No.	*Title*	*Page*
1	*Comparison between confirmed, and control groups as regard. Patients' characteristics in both study groups*	**67**
2	*Comparison between confirmed, and control groups as regard. AFI and β-hCG in vaginal wash in both study groups*	**68**
3	*ROC curve analysis for discrimination between cases with confirmed PROM and controls using vaginal β-hCG*	**70**

List of figures:

Fig. No.	*Title*	*Page*
1	*Formation of the amnion.*	9
2	*Development of the chorion and amniochorionic membrane*	*11*
3	*Schematic representation of the structure of the fetal membranes at term.*	*12*
4	*Water circulation between the fetus and amniotic fluid*	*14*
5	*Normal range of AF volume in human gestation*	*15*
6	*Hypothesis of preterm premature rupture of membrane shows possible separation between its causes and effects.*	*24*
7	*Diagram of the diverse pathologies that can potentially cause preterm labor, preterm premature rupture of the fetal membranes, or cervical ripening.*	*25*
8	*AmniSure® ROM test for the diagnosis of ruptured fetal membrane*	*38*
9	*Box plot showing the AFI in patients with confirmed PROM and controls. Box represents the range from the 1st quartile to 3rd quartile. Line inside the box represents the median (2nd quartile). Error bars represent the minimum and maximum values.*	*68*
10	*Box plot showing β-hCG concentration in vaginal wash in patients with confirmed PROM and controls. Box represents the range from the 1st quartile to 3rd quartile. Line inside the box represents the median (2nd quartile). Error bars represent the minimum and maximum values.*	*69*
11	*ROC curve for discrimination between cases with confirmed PROM and controls using vaginal β-hCG.*	*71*
12	*Sensitivity and specificity of various vaginal β-hCG cut-off values for discrimination between cases with confirmed PROM and controls.*	*72*

PROTOCOL

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INTRODUCTION

Prelabor 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 which occurs in pregnancy when the amniotic sac ruptures before 37 weeks of gestation **(Deering et al., 2007).**

Premature rupture of the membranes (PROM) occurs in 10% of all gestations and about 2–4% of preterm pregnancies, with complications such as infection and preterm birth (**Kafali and Oksuzler, 2007**). Fetal outcome is highly compromised when PROM occurs at young gestational age and anhydramnios is prolonged. (**Hunter et al., 2012**).

Spontaneous membrane rupture occurs physiologically at term either before or after the onset of symptomatic contractions. This is believed to be related to progressive weakening of the membranes seen with advancing gestation, largely due to collagen remodeling and cellular apoptosis. When PROM occurs before term, the process of membrane weakening may be accelerated by a number of factors such as stretch, Infection, inflammation and local hypoxia (**Mercer, 2010**).Numerous risk factors are associated with PROM as smoking, low socioeconomic status, negros , history of sexually transmitted infections, history of previous preterm delivery, uterine over distension (e.g. polyhydramnios and multiple pregnancy), but the most important risk factors are previous preterm labor and previous PROM. (**Canavan et al., 2004 a)**.

There is evidence demonstrating an association between ascending infection from the lower genital tract and PROM. In women with PROM about one-third of pregnancies have positive amniotic fluid cultures and

studies have shown that bacteria have the ability to cross intact membranes **(Penney, 2008).**

Diagnosis of PROM is easy when there is a demonstration of amniotic fluid leakage from the cervix, but more difficult when there is doubt as to whether PROM has occurred or not. Failure to identify patients with membrane rupture can result in failure to implement obstetric measures, while the false diagnosis can lead to inappropriate interventions such as hospitalization or labor induction **(Kim et al., 2005).** However, in 10% of cases, PROM diagnosis might be difficult when the patient reports tiny and/or intermittent fluid discharge and ultrasound examination shows a normal amniotic fluid index. In these specific cases, noninvasive biochemical tests based on the detection of amniotic fluid proteins in the vagina using immunochromatography could be helpful. These tests are based on the detection of proteins with high expression level in amniotic fluid compared with other physiological fluids such as maternal blood, cervicovaginal secretion, urine and seminal fluid **(Doret et al., 2013).**
These tests include the 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. All these tests have advantages and drawbacks. Up till now there is no gold standard diagnostic test for PROM (**Kafali and Oksuzler, 2007**).

The beta subunit of human chorionic gonadotropin (β-hCG) has been evaluated as a possible predictor of preterm delivery and as a marker for PROM.Human chorionic gonadotropin is produced by syncytiotrophoblasts, and is present in varying degrees in serum, urine, and amniotic fluid during pregnancy. Previous investigators have established quantitative ranges and thresholds of HCG concentrations in

pregnant women with and without ruptured membranes during each trimester (**Bahasadri et al., 2013**).

AIM OF THE WORK

To determine whether the measurement of beta-human chorionic gonadotropin (β-hCG) levels in vaginal fluid is accurate for the diagnosis of premature rupture of membranes (PPROM).

PATIENTS AND METHODS

Site of the study:

This prospective case control study was conducted in Ain Shams Maternity Hospital.

Patients:

After explaining the method to the patients and taking an informed consent, it was performed on 60 pregnant women divided into 2 groups as follows

Group I (Confirmed PROM group)

It included 30 pregnant women with PPROM with the following inclusion criteria:

1. GA completed 24 weeks to completed 36 weeks .
2. Single intrauterine pregnancy.
3. History of watery vaginal leakage.
4. Visualization of amniotic fluid leakage (sterile cusco speculum examination: positive fluid leakage).

Group II (Control group)

It included 30 pregnant women who were attended the outpatient clinic for routine antenatal care with following inclusion criteria:

1. GA completed 24 weeks to completed 36 weeks.
2. Single intrauterine pregnancy.
3. Healthy pregnant women.
4. No history of vaginal fluid leakage.
5. Average amount of amniotic fluid index: AFI: 10-15 cm.

Exclusion Criteria:

1. Fetal distress (diagnosed by CTG).
2. Fetal anomalies.
3. IUFD