

Sonographic assessment of myometrial thickness as a predictor for the latency interval in women with preterm premature rupture of membranes and oligohydramnios

Thesis

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BY

Tamer Mohamed Essam EL-Din Youssef

Master degree in obstetrics and gynecology

Specialist of Obstetrics and gynecology Helwan Hospital

Under supervision of

Professor. Mostafa Mahmoud Asem

Professor of Obstetrics and Gynecology

Faculty of Medicine -Cairo University

Dr. Ahmed Mahmoud Al sayed ALI

Assistant Professor of Obstetrics and Gynecology

Faculty of Medicine -Cairo University

Dr. Sherine Hosny Mohamed

Lecturer of Obstetrics and Gynecology

Faculty of Medicine -Cairo University

Faculty of Medicine -Cairo University

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا

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Aim of Work

The aim of this work is to measure the myometrial wall thickness (MT) by ultrasound scanning in patients with preterm premature rupture of membranes as a predictor for the latency interval, for better assessment and management of this situation with less complication.

ABSTRACT

Objective: Term labor is associated with global thinning of the myometrium. We hypothesized that a thickened myometrium at the time of preterm premature rupture of membranes (PPROM) predicts less myometrial wall stress and, consequently, a longer latency interval.

Study design: Myometrial thickness was measured prospectively in 100 pregnant women enrolled in the following groups: preterm premature rupture of membranes (**PPROM**), preterm non-labor control group (**P-CTR**), and term non-labor control (**T-CTR**). All preterm premature rupture of membranes (**PPROM**) women had oligohydramnios. Myometrial thickness was measured ultrasonographically at the midanterior, fundal, posterior, and lower uterine segment wall in cases and controls.

Conclusion: Significant thickening of the anterior and fundal walls of the uterus follows preterm premature rupture of membranes (**PPROM**). A thick myometrium in non-laboring patients with PPRM is associated with longer latency interval. Sonographic evaluation of MT may represent an alternative clinical tool for the prediction of a short latency interval in women with preterm premature rupture of membranes (**PPROM**).

KEY WORDS:

PPROM, Myometrium, Oligohydramnios Ultrasound preterm birth, latency interval.

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List of abbreviation

ACD	Advanced cervical dilatation
AFI	Amniotic fluid index
AFP	Alpha fetoprotein
AFV	Amniotic fluid volume
BV	Bacterial vaginosis
CF	Cervical. funneling
CI	Confidence interval
CL	Cervical length
CRP	C-reactive protein
FBM	Fetal breathing movement
fFN	Fetal fibronectin
GBS	Group B-streptococci
HCG	Human chorionic gonadotropin
OH	Hydroxyl ion
IGFBP	Insulin-like growth factor Binding protein
IL	Interleukin
IUFD	Intrauterine fetal death
IUGR	Intrauterine growth restriction
LOX	Lysyl oxidase
LUS	Lower uterine segment
MMP	Matrix, metalloproteinase
MT	Myometrial thickness
NEC	Necrotizing enterocolitis
NO	Nitric oxide
PPROM	preterm premature rupture of membranes
RDS	Respiratory distress syndrome
ROS	Reactive oxygen species
SEFW	Sonographic estimation of fetal weight
SHE-IVH	Subependymal hemorrhage-intra-ventricular hemorrhage
TAT	Thrombin antithrombin
TIMP	Tissue inhibitors of metalloproteinase
TNF	Tumor necrotic factor
P-CTR	preterm control
T-CTR	Term control

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Introduction

Spontaneous rupture of membranes is a normal component of labor and delivery. Rupture of membranes before the onset of labor is considered premature (PROM), and induction of labor is common if the patient is at or close to term. Patient management always becomes more challenging when rupture of membranes occurs preterm (PPROM), and in the absence of labor. The natural history of PROM progresses in such a way that 90% of term patients and 50% of preterm patients enter spontaneous labor within 24 hours. The major question regarding management of these patients is whether to allow them to enter labor spontaneously or to induce labor. In large part, the management of these patients depends on their desires (*Morales et al, 1993*).

Many cases of PPRM are caused by idiopathic weakening of the membranes (*Deyer et al., 2000*). Other causes include incompetent cervix, abruption placenta, and amniocentesis. The incidence of PPRM ranges from 2% to 20% and is associated with 18% to 20% of perinatal deaths (*Mercer, 2003*).

Perinatal risks with PPRM are primarily complications from immaturity including respiratory distress syndrome, intraventricular Hemorrhage, patent ductus arteriosus, and necrotizing enterocolitis (*Mercer et al., 1997*).

Pulmonary hypoplasia is the most serious complications, and can be lethal, the presence of severe (AFI less than 2 cm), prolonged (more than 14 days), and early (less than 25 weeks at onset) oligohydramnios has been associated with a neonatal mortality rate greater than 90% (*Johnson et al., 1981*).

The incidence of stillbirth subsequent to PPRM ranges from 3.8% to 21.7%, this increased rate of death may be explained by increased susceptibility of the

umbilical cord to compression or of the fetus to hypoxia and intrauterine infection (*Hailiday et al., 2000*).

Similar to myocardium, the force of labor is uterine wall tension opposed to the resistance of the cervix, perineum and pelvis (*Buhimschi et al., 2003*). Mathematical modeling reveals that uterine wall stress (defined as applied force per unit cross-sectional area of material) is directly proportional to both the intracavitary pressure and the radius of the curvature, but inversely proportional to the thickness of the myometrium (*Deyer et al., 2000*). Thus, the thicker the myometrium, the lower the uterine wall stresses.

Although scientists have long investigated "the timing of birth", the understanding of biological mechanisms regulating the events that prevent and initiate labor remains limited (*Normitz et al., 1999*).

Sonographic observation that the myometrium thins symmetrically during active labor with the least amount of thinning at the uterine fundus stimulate scientists to rethink the mechanisms responsible for the uniform dispersion of the contractile forces that insure efficient fetal expulsion. Sudden decompression with the uterine sac, which has been filled with a minimally compressible fluid that normally opposed thickening, is the most likely physiologic explanation (*Hailiday et al., 2000*).

A direct correlation was found between fundal myometrial thickness (MT) and the latency interval (LI). Showing that the thicker the fundal myometrium, the longer the latency interval (*Buhimschi et al.2005*).

The latency interval is defined as the time period (days or hours) from the time of rupture of membranes reported by the patients to delivery. Our understanding of the mechanisms that determined the length of the latency interval

after PPROM is hindered by the fact that the human myometrium and cervix appear to have redundant and parallel mechanisms to ensure adequate length of gestation (*Buhimschi et al., 2003*). Furthermore the impact of pregnancy and labor on the uterus and cervix differs greatly (*Buhimschi et al, 1996*).

The prevailing theories surrounding PPROM latency interval may overestimate the importance of the cervix, leaving the role played by myometrial activation largely unexplored (*Prichard et al., 1980*). The digital cervical examination and frequency of uterine contractions have weak prognostic values (*Iams et al., 2003*). Not only are digital cervical examination of women with PPROM and frequency of uterine contractions poorly predictive, but a digital exam may actually increase the risk of ascending infection.

There has been much attention focused on the sonographic assessment of cervical length since shortening is associated with an increased risk of preterm delivery in both nulliparous and multiparous women (*Weish et al., 2002*). Sonographic evaluation of cervical length in women with PPROM is reported to have maximum sensitivities and specificities of 63% and 81% respectively (*Bergelin et al., 2001*).

One of the most important factors that predict the latency interval rather than cervical length is oligohydramnios. Women with PPROM and oligohydramnios at less than 25 weeks deliver earlier compared to those with adequate amniotic fluid volume. It is thus not surprising to find that 85% of women with adequate amniotic fluid deliver beyond 25 weeks, and have much lower neonatal morbidity and mortality rates (*Vermillion et al. 2000*).

It is assumed that women with a long latency interval after spontaneous PPROM are in a state of myometrial quiescence or incomplete myometrial activation, and it is demonstrated that the long latency and presumed myometrial quiescence are associated with a greater thickness of the anterior and fundal wall myometrium. It is possible that those women with PPROM and thin myometrium

already experienced functional complete myometrial activation that allows for coordinate tone, contractions, and shorter latency interval (*Buhimschi et al., 2005*).

There are insufficient data at this time to determine how myometrial thickness (MT) changes longitudinally over the course of the latency period in women who undergo spontaneous onset of uterine contractions. Further, it is still unknown the appropriate method to predict latency in women with PPROM (*Buhimschi et al., 2003*).

Studies combining cervical length and myometrial thickness sonography, fetal fibronectin, proteomic analysis of the amniotic fluid at the time of PPROM and development of highly sensitive noninvasive uterine contraction monitoring methods are warranted (*Buhimschi et al., 2003*).

Transabdominal ultrasound evaluation of myometrial thickness and surface electromyographic analysis of uterine contraction remain the only noninvasive methods to evaluate choriodecidual myometrial activation, and thus predicting the latency interval (*Pritchard et al., 1980*).

Aim of the work

The aim of this work is to measure the myometrial wall thickness (MT) by ultrasound scanning in patients with preterm premature rupture of membranes as a predictor for the latency interval.

Patients and Methods

The present study will be carried out at AL Kasr Al Ainy hospital during the period from January 2013 to August 2014. We will approach women admitted to the labor and delivery ward and to the ante partum in-patient high risk service.

After proper counseling, all women solicited for enrollment will agree to participate and provide written informed consent. The total number of pregnant women enrolled in the study will be 100 women. These will be divided into three groups:

- **Group I:** included 50 women with preterm premature rupture of membranes (**PPROM**, n=50) with gestational age from 24 to 34 weeks.
- **Group II:** included 25 term non-labor control (**T-CTR**, n=25) with gestational age from 37 to 40 weeks.
- **Group III:** included 25 preterm non-labor control (**P-CTR**, n=25) with gestational age from 24 to 34 weeks.

Inclusion criteria for women at enrollment will include women with singleton pregnancy for the three groups and with a definite history of current PPRM for the study group.

Exclusion criteria for the three groups included:

- 1 - Suspected fetal growth restriction (IUGR).
- 2- Any gross fetal anomalies.
- 3- Abnormalities of placentation.
- 4- Uterine structural abnormalities.
- 5-Fetal jeopardy or intrauterine fetal death (IUFD).

Exclusion criteria for women with PPRM

All of the above criteria and other specific criteria as:

Protocol _____

- 1-Women presenting with chorioamnionitis with fever over 38C°, abdominal tenderness, foul vaginal discharge and/or fetal tachycardia
- 2-Diabetics, immunocompromized and cardiac patients.
- 3- Women with cervical circlage.
- 4-Women with drained liquor.

All women will be subjected to:

(1)History:

Full history will be taking from all women including personal history for maternal age, obstetric history for number of previous pregnancies, history of previous PPRM.

History of present pregnancy included gestational age, history of drug intake during the present pregnancy with special emphasis for women with PPRM giving history of gush of clear watery fluid from the vagina.

Past history will be useful to exclude women with a contraindication for conservative management in the study group.

(2)Physical examinations:

General examination will be done for the three groups for pulse, arterial blood pressure and temperature to exclude any signs of chorioamnionitis in the study group.

Abdominally, fundal level examinations for the three groups will be done for predicting the gestational age and/or, IUGR abnormalities of liquor. Monitoring of uterine contraction will help to pick up women who are not in labor in the study group.