Fetal Adrenal Gland Enlargement A Novel Accurate Predictor of Preterm Birth

Thesis

Submitted for partial fulfillment of the master degree
In Obstetrics and Gynecology

By:

Nesma Nour El-din Abo El-ela Mohamed
M.B.B.Ch (2008)
Ain Shams University
Resident of Obstetrics & Gynecology

Supervised by

Dr. Moustafa Ibrahim Ibrahim
Assistant Professor of Obstetrics & Gynecology
Faculty of Medicine, Ain Shams University

Dr. Ahmed Shiref Abd El-Hamid
Lecturer of Obstetrics & Gynecology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2013


بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا
عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ
صدق الله العظيم
سورة البقرة آية (32)

Acknowledgement

First, all due thanks are to **Allah** *for blessing this work till it has reached its end, as a part of his generous help throughout my life.*

I would like to express my immense gratitude and appreciation to **Dr. Moustafa Ibrahim Ibrahim** *Assistant professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for the great support and encouragement he gave me throughout the whole work. It is a great honor to work under his guidance and supervision.*

I am greatly honored to express most thanks to **Dr. Ahmed ShirefAbd el-Hamid** *Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his close supervision, continuous help and his tremendous efforts in the meticulous revision of the whole work.*

With great pleasure I am also grateful to **Dr. Mohamed Kamal Atman** *Fellow of Ultrasound and Fetal Special Care Unit, Faculty of Medicine Ain Shams University, for his kind effort and support in doing the ultrasonography for the patients. He offered me a lot of help and encouragement.*

My deepest gratitude to **Dr. Mohamed Elkady** *Assistant professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University and to* **Dr. Ahmed Elhusseiny** *Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University for Their valuable scientific contribution .*

Finally, I am thankful to my family for their support throughout my life and this work.

NesmaNour El-din Abo El-ela

Contents

List of Abbreviations i

List of Tables iii

List of Figures iv

Introduction and Aim of the Work 1

Chapter 1: Preterm Labor 4

Chapter 2: Complications of Preterm Labor..... 14

Chapter 3: Prediction of Preterm Labor..... 21

Chapter 4: Fetal Adrenal Gland as A Predictor of Preterm Labor 30

Patients and Methods..... 41

Results..... 50

Discussion..... 65

Summary..... 72

Conclusion 74

Recommendations 75

References..... 76

Arabic Summary ..... --

List of Abbreviations

ACTH	:	Adrenocorticotropin
AF	:	Amniotic fluid
AGV	:	Adrenal gland volume
BMI	:	Body mass index
BPD	:	Bronchopulmonary dysplasia
BV	:	Bacterial vaginosis
CAGV	:	Corrected adrenal gland volume
CL	:	Cervical length
CLD	:	Chronic lung disease
COX	:	Cyclo-oxygenase
CP	:	Cerebral palsy
CRH	:	Corticotrophin-releasing hormone
DES	:	Diethylstilbestrol
DHEAS	:	Dehydroepiandrosterone sulfate
E1	:	Estrone
E2	:	Estradiol
E3	:	Estriol
Ffn	:	Fetal fibronectin
FHR	:	Fetal heart rate
GA	:	Gestational age
GBS	:	Group B streptococcus
HCG	:	Human chorionic gonadotropin
HPA	:	Hypothalamic-pituitaryadrenal axis
HUAM	:	Home uterine activity monitoring
IL	:	Interleukin
IUGR	:	Intrauterine growth retardation
LBW	:	Low birth weight
MFMN	:	Maternal-Fetal MedicineUnitNetwork
MMP	:	Matrix metalloproteinase
PG	:	Prostaglandin
PPROM	:	Preterm premature rupture of membrane
PTB	:	Preterm birth

List of Abbreviations (Cont.)

PTL	:	Preterm labor
RDS	:	Respiratory distress syndrome
ROP	:	Retinopathy of prematurity
SPB	:	Spontaneous preterm birth
TFP	:	Transfundal pressure
TNF	:	Tumor necrosis factor
TVU	:	Transvaginal ultrasound
VOCAL	:	Virtual Organ Computer-aided AnaLysis
WHO	:	World Health Organization

List of Tables

Table	*Table title*	*Page*
1	Demographic data, delivery outcomes and sonographic characteristics according to delivery interval	51
2	Accuracy of fetal zone dimension ratios as predictors of preterm birth within 7 days	54
3	Study parameters finding according to delivery interval	55
4	Correlation between measurement-to-delivery Interval and each of cervical length, cAGV and fetal zone width	56
5	Accuracy of cervical length, fetal adrenal gland volume and fetal zone enlargement, cervicovaginal fibronectin as predictors of delivery within 7 days	63
6	Summary of the previous studies	64

List of Figures

Fig.	*Title*	*Page*
(1)	**(a)**Transabdominal and **(b)**transvaginal ultrasound cervical length measurement of the same patient	27
(2)	schematic and ultrasonographic representation of cervical funneling	28
(3)	shape of adrenal glands	31
(4)	blood supply of adrenal glands	32
(5)	Embryology of adrenal glands	33
(6)	Extra-adrenal regulation	35
(7)	Multiplanar technique for the measurement of the adrenal gland volume using VOCAL software	39
(8)	Methodology of measurement of the whole adrenal gland and the fetal zone	40
(9)	Patient was admitted with preterm labor at 28w, shows fetal adrenal gland volume 1.08 cm3 and fetal zone 20% .	45
(10)	Patient was admitted with preterm labor at 34w, shows fetal adrenal gland volume 1.82 cm3 and fetal zone 31%.	45
(11)	Patient was admitted with preterm labor at 30w, shows fetal adrenal gland volume 1.69 cm3 and fetal zone 43%.	46
(12)	Patient was admitted with preterm labor at 33w, shows enlarged fetal adrenal gland of volume7.40cm3 and fetal zone 65%.	46

List of Figures

Fig.	*Title*	*Page*
Results list of figures		
(1)	Participants flow-chart	50
(2)	Pie-Chart showing Timing of Delivery in Included Women	53
(3)	Box-Plot Chart showing Difference between Women who Delivered within 7 days and those who Delivered beyond 7 days regarding Cervical Length	57
(4)	Box-Plot Chart showing Difference between Women who Delivered within 7 days and those who Delivered beyond 7 days regarding Fetal Adrenal Gland Volume	58
(5)	Box-Plot Chart showing Difference between Women who Delivered within 7 days and those who Delivered beyond 7 days regarding Fetal Zone Enlargement Percentage	59
(6)	ROC Curves for Cervical Length, Fetal Adrenal Gland Volume and Fetal Zone Enlargement as Predictors of Delivery within 7 days	61

Introduction

Preterm birth (PTB) is one of the leading causes of neonatal morbidity and mortality ***(Goldenberg et al., 2008).***

Hence, there is growing interest in the identification of women who are at risk for spontaneous PTB. Many biophysical and biochemical markers have been discovered to identify those women who are at risk for spontaneous PTB. These markers include 2-dimensional (2D) measurement of cervical length (CL), cervicovaginal fetal fibronectin and salivary estriol ***(Honest et al., 2009)***.

There is a need for an accurate method with high sensitivity and specificity for prediction of preterm labor, so that an appropriate management or referral to a higher center can be done in women likely to have PTB, whereas unnecessary tocolytic therapy can be avoided in women who are unlikely to have PTB ***(Rengaraj et al., 2009)***.

Literature has suggested that activation of the fetal hypothalamic-pituitary-adrenal axis play a crucial role in commencement of labor ***(Norwitz et al., 1999).***

Abnormal activation of labor cascade in preterm delivery leads to increased *dehydroepiandrosterone-sulfate* (DHEAS) *production in the central* zone of the fetal adrenal

gland .This increase in central fetal zone leads to enlargement of whole fetal adrenal gland ***(Langlois et al.,2002).***

A previous study demonstrated that 3-dimensional (3D) ultrasound measurement of fetal adrenal gland volume (AGV) may identify women at risk for impending PTB ***(Turan et al.,2007).***

A recent study has concluded that 2-dimensional measurement of fetal zone enlargement (FZE) offers the potential to accurately anticipate PTB within 7 days. This anticipation is equal to the more complex 3D volume measurement ***(Turan et al.,2011).***

In a more recent study receiver operator characteristics (ROC) curve analysis revealed that, 3-D cAGV was superior to 2-D cAGV for anticipation of PTB within 7 days of the scan ***(Turan et al., 2012).***

Aim of the Work

The aim of the current study is to assess the diagnostic accuracy of 3-dimensional ultrasound-measurement of fetal adrenal gland volume (AGV) and fetal zone enlargement (FZE) as predictors of preterm birth in comparison to cervical length (CL) and cervicovaginal fetal fibronectin.

Chapter I

Preterm Labor

Definition:

Preterm birth, defined as birth at less than 37 weeks or 259 days of gestation from the 1st day of the last menstrual period, is the most important single determinant of adverse infant outcome in terms of both survival and quality of life ***(RCOG2011)*.**

The morbidity associated with preterm birth often extends to later life, resulting in lifelong physical, neurological, or educational disability, often at great cost to families and society***(WHO 2012).***

Epidemiology of Preterm Labor

1-Age and parity:

Both extremes of maternal age have been associated with an increased risk of preterm birth ***(Kogan et al., 2002; Gortzak-Uzan et al., 2001).***

Preterm delivery is commonerin first pregnancies and the risk decreases with successive pregnancies ***(Tough et al., 2001***).

Racial differences seem to be clear according to all studies; with black women having higher preterm birth rates ***(Savitz et al., 1991***).

2-Socioecnomic Status and genetic factors:

Lower social class has been found to be a risk factor for prematurity in many studies ***(Johnson et al., 2002).***

A low prepregnancy body mass index (BMI) was strongly associated with an increased risk of preterm birth ***(Goldenberg et al., 1998)*** and obese women were at a markedly decreased risk of spontaneous preterm birth ***(Hendler et al., 2005).***

A more recent study has shown a stronger relation between smoking and preterm birth resulting from prelabor rupture of the membranes ***(Savitz et al., 2001).***

Recent attention has focused on the potential for genetic epidemiology to contribute to understanding of preterm labor. Polymorphisms of certain critical genes may be responsible for a harmful inflammatory response in those who possess them ***(Holst and Garnier., 2008).***

3-Physical Activity and Psychological Factor:

Heavy physical work, prolonged standing and shift and night work are all associated with preterm birth ***(Mozurkewich et al., 2000).***

Anxiety has been found to be related to preterm labor, but the association was weaker in those women who had no

pregnancy-related morbidity to worry about ***(Doyle et al., 2003).***

4-Obstetric History:

Previous preterm delivery:

A previous preterm delivery is the most significant risk factor for subsequent preterm delivery and the relative risk increases with the number of prior preterm Births ***(Bloom et al., 2001).***

Previous preterm premature rupture of membranes:

The risk of preterm delivery in women with previous PPROM has been estimated to range from 34% to more than 44%, and the risk of recurrent preterm rupture of the membranes to range from 16% to 32%***(Lee et al., 2003).***

Previous abortion:

Threatened miscarriage in the first trimester has been associated with preterm delivery in a large US prospective study***(Weiss 2004).***

Interpregnancy interval:

Women in with inter-pregnancy intervals of <12 months were at increased risk for a preterm birth in the subsequent pregnancy***(Hsieh* et al., *2005***).