



Predictive Accuracy of Three Dimensional Ultrasound Measurement of Fetal Adrenal Gland Volume in Preterm Labor Cases

Thesis

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

By

Abdurrahman Hussien Mohammed

M.B.B.Ch, Faculty of Medicine - Minia University, 2012

Under Supervisors

**Prof. Dr. Waleed Hitler Ahmed
El-Tantawy**

Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Dr. Mai Medhat Nawara Mohyi ElDin

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

**Faculty of Medicine
Ain Shams University
2019**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



ACKNOWLEDGEMENT

First of all, thanks to **Allah** whose magnificent help was the main factor in completing this work.

No words could express my deepest thanks and appreciation to **Prof. Dr. Waleed Hitler Ahmed El-Tantawy**, Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for inspiring me with the idea of this work. His patience, precious advice and guidance enlightened my way throughout this work.

I want also to express my profound gratitude to **Dr. Mai Medhat Nawara Mohyi ElDin**, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for her patience, valuable advice and continuous help in completing this work.

Finally, my deepest thanks to all my family and colleagues who helped me in the production of this work.

Contents

Subjects	Page
List of abbreviations.....	II
List of figures.....	IV
List of tables.....	VI
• Introduction	1
• Aim of the Work	4
• Review of Literature	
♦ Chapter (1): Preterm Labor	5
♦ Chapter (2): Complications of Preterm Labor	18
♦ Chapter (3): Prediction of Preterm Labor	25
♦ Chapter (4): Fetal Adrenal Gland as A Predictor of Preterm Labor	42
• Patients and Methods	53
• Results	64
• Discussion	81
• Summary	89
• Conclusion	91
• Recommendations	92
• References	93
• 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

List of Abbreviations

IL	:	Interleukin
IUGR	:	Intrauterine growth retardation
LBW	:	Low birth weight
MFMN	:	Maternal-Fetal Medicine Unit Network
MMP	:	Matrix metalloproteinase
PG	:	Prostaglandin
PPROM	:	Preterm premature rupture of membrane
PTB	:	Preterm birth
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 Figures

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>1</u>	a)Transabdominal and (b)transvaginal ultrasound cervical length measurement of the same patient.	38
<u>2</u>	Schematic and ultrasonographic representation of cervical funneling.	39
<u>3</u>	Shape of adrenal glands.	43
<u>4</u>	Blood supply of adrenal glands.	44
<u>5</u>	Embryology of adrenal glands.	45
<u>6</u>	Extra-adrenal regulation.	47
<u>7</u>	Multiplanar technique for the measurement of the adrenal gland volume using VOCAL.	51
<u>8</u>	Methodology of measurement of the whole adrenal gland and the fetal zone.	52
<u>9</u>	Patient was admitted with threatened preterm labor at 32w, shows fetal adrenal gland volume 1.08 cm ³ and fetal zone 20%.	57
<u>10</u>	Patient was admitted with threatened preterm labor at 34w, shows fetal adrenal gland volume 1.82 cm ³ and fetal zone 31%.	58
<u>11</u>	Patient was admitted with threatened preterm labor at 35w, shows fetal adrenal gland volume 1.69 cm ³ and fetal zone 43%.	58
<u>12</u>	Patient was admitted with threatened preterm labor at 33w, shows enlarged fetal adrenal gland of volume 7.40cm ³ and fetal zone 65%.	59
<u>13</u>	Flow chart.	64

List of Figures

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>14</u>	Bar chart between delivery interval $\leq 7d$ and $>7d$ according to corrected adrenal gland volume.	68
<u>15</u>	Bar chart between delivery interval $\leq 7d$ and $>7d$ according to fetal zone enlargement.	69
<u>16</u>	Bar chart between delivery interval $\leq 7d$ and $>7d$ according to cervical length.	70
<u>17</u>	Bar chart between delivery interval $\leq 7d$ and $>7d$ according to fetal fibronectin.	71
<u>18</u>	Pie-chart showing timing of delivery in included women.	73
<u>19</u>	Bar chart study parameters finding according to delivery interval.	76
<u>20</u>	ROC curves for cervical length, corrected fetal adrenal gland volume and fetal zone enlargement and cervicovaginal fetal fibronectin as predictors of delivery within 7days.	80

List of Tables

<u>No.</u>	<u>Table</u>	<u>Page</u>
<u>1</u>	Risk of preterm delivery.	26
<u>2</u>	Comparison between delivery interval $\leq 7d$ and $>7d$ according to demographic data.	65
<u>3</u>	Comparison between delivery interval $\leq 7d$ and $>7d$ according to obstetric history and pregnancy outcome.	66
<u>4</u>	Comparison between delivery interval $\leq 7d$ and $>7d$ according to sonographic data.	67
<u>5</u>	Accuracy of fetal zone dimension ratios as predictors of preterm birth within 7 days.	74
<u>6</u>	Study parameters finding according to delivery interval.	75
<u>7</u>	Correlation between measurement- to-delivery interval and each of cervical length, cAGV and fetal zone width.	77
<u>8</u>	Accuracy of cervical length, fetal adrenal gland volume and fetal zone enlargement, cervicovaginal fibronectin as predictors of delivery within 7 days.	79

Introduction

Preterm labor is defined as delivery before the completion of 37 weeks of gestation (*Allaire et al., 2001*).

It occurs in 7-12% of all deliveries and account for over 85% of perinatal morbidity and mortality (*Tucker et al., 1991*).

When neonatal mortality rates are reviewed, it has been found that 83% of these rates correspond to the babies born before 37th week of gestation (*Copper et al., 1993*).

Hence, there is growing interest in the identification of women who are at risk for spontaneous preterm birth (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*).

Convincing data has shown that transvaginal cervical length measurement can identify women at high risk of preterm labor and therefore it is widely used in risk estimation (*Abdelazim and Abu Faza, 2012*).

However, as understanding the mechanism of preterm birth has evolved, obstetricians have learned that in some women, cervical shortening carries no increased risk of occurrence of labor (*Lim et al., 2011*).

Literature has suggested that activation of fetal hypothalamic pituitary adrenal axis as response to fetal distress plays a crucial role in commencement of labor in women at risk of PTB (*Norwitz et al., 1999*).

During preterm labor, activation of labor cascade leads to increased dehydroepiandrosterone sulphate (DHEAS) production in central zone of fetal adrenal gland with subsequent increase in whole gland size (*Langolis 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 our study is to assess the accuracy of 3D fetal adrenal gland volume measurement in predicting the occurrence of labor in women presented with symptoms of threatened preterm labor (PTL).

Chapter (1)

Preterm Labor

Definition:

Preterm labor is defined as presence of regular successive uterine contractions of sufficient frequency and intensity that lead to cervical changes in the form of dilatation and/or effacement before 37 weeks of gestation (*Ross and Eden 2009*).

Incidence:

Preterm labor occurs in 7-12% of all deliveries and accounts for over 85% of perinatal morbidity (*Tucker et al., 1991*).

Of all preterm births 40-50% of them occurs spontaneously, with the remaining occur as a result of preterm premature rupture of membranes (25-40%) and induced preterm labor due to medical or obstetrical conditions as severe pre-eclampsia, antepartum hemorrhage and growth restriction (20-25%) (*Iams, 2002*).

Classification:

Preterm labor is classified according to gestational age into:

- Moderate preterm labor (32-36₊₆ weeks).
- Late preterm labor (34-36 weeks).
- Very preterm labor (28-32 weeks).
- Extremely preterm (<28 weeks).

And according to birth weight into:

- Low birth weight (<2500 grams).
- Very low birth weight (<1500 grams).
- Extremely low birth weight (<1000 grams) (**WHO 2012**).

Risk factors for preterm labor:

1. Age and race:

Women who get pregnant at ages less than 18 years old or more than 35 years old are at high risk of preterm birth (*Goldenberg et al., 2008*).

Racial association is also noticed as risk of preterm birth increases up to 15-18% in Afro-Americans and Afro-Caribbean women which remains unexplained (*Goldenberg et al., 2008*).