

# **SURVEY OF PREDICTION AND MANAGEMENT OF SPONTANEOUS PRETERM LABOR**

*A thesis*

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# مسح عن التنبؤ وكيفية معاملة الولادة المبكرة التلقائية

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### **List of Abbreviations**

|             |                                                                 |
|-------------|-----------------------------------------------------------------|
| ACOG.....   | American College of Obstetricians and Gynecologists             |
| AF.....     | Amniotic fluid                                                  |
| BCIN.....   | 5-bromo-4-chloro-3-indolyl- $\alpha$ -D-N-acetylneuraminic acid |
| BMI.....    | Body mass index                                                 |
| BV.....     | Bacterial vaginosis                                             |
| cAMP.....   | Cyclic adenosine monophosphate                                  |
| CBG.....    | Corticosteroid-binding globulin                                 |
| cDNA.....   | Complementary deoxyribonucleic acid                             |
| cGMP.....   | Cyclic guanosine monophosphate                                  |
| CNS.....    | Central nervous system                                          |
| COX II..... | Cyclooxygenase type II                                          |
| CP.....     | Cerebral palsy                                                  |
| CRH.....    | Corticotrophin-releasing hormone                                |
| CS.....     | Cesarean section                                                |
| D&C.....    | Dilatation and curettage                                        |
| DES.....    | Diethylstilbestrol                                              |
| DM.....     | Diabetes mellitus                                               |
| DNA.....    | Deoxyribonucleic acid                                           |
| ECG.....    | Electrocardiograph                                              |
| ECV.....    | External cephalic version                                       |
| ELISA.....  | Enzyme linked immunosorbent assay                               |
| EPI.....    | Epithelial cells                                                |
| FDA.....    | Food and drug administration                                    |
| fFN.....    | Fetal fibronectin                                               |
| FIRS.....   | Fetal inflammatory response syndrome                            |
| GRK.....    | Gestational-related kinases                                     |
| hCG.....    | human chorionic gonadotropin                                    |
| HIV.....    | Human immunodeficiency virus                                    |
| HMD.....    | Hyaline membrane disease                                        |
| HSG.....    | Hysterosalpingogram                                             |
| HUAM.....   | Home uterine activity monitoring                                |
| ICH.....    | Intracranial hemorrhage                                         |
| ICU.....    | Intensive care unit                                             |
| IFN.....    | Interferon                                                      |
| Ig.....     | Immunoglobulin                                                  |

|                     |                                                           |
|---------------------|-----------------------------------------------------------|
| IL.....             | Interleukin                                               |
| IL-1Ra.....         | Interleukin-1 receptor antagonist                         |
| IM.....             | Intramuscular                                             |
| IUFD.....           | Intrauterine fetal death                                  |
| IUGR.....           | Intrauterine growth restriction                           |
| IV.....             | Invitro fertilization                                     |
| IVF.....            | Intravenous                                               |
| IVH.....            | Intraventricular hemorrhage                               |
| LBW.....            | Low birth weight                                          |
| LDH.....            | Lactate dehydrogenase                                     |
| LMP.....            | Last menstrual period                                     |
| LPS.....            | Lipopolysaccharide                                        |
| MCP.....            | Monocyte chemoattractant protein                          |
| MIP.....            | Macrophage inflammatory protein                           |
| MLCK.....           | Myokine light-chain kinase                                |
| MMP.....            | Matrix metalloproteinase                                  |
| MRI.....            | Magnetic resonance imaging                                |
| mRNA.....           | Messenger ribonucleic acid                                |
| NEC.....            | Necrotizing enterocolitis                                 |
| NO.....             | Nitric oxide                                              |
| NOS.....            | Nitric oxide synthase                                     |
| NSAID.....          | Non-steroidal anti-inflammatory drugs                     |
| PAF.....            | Platelet activating factor                                |
| PDA.....            | Patent ductus arteriosus                                  |
| PDE.....            | Phosphodiesterase                                         |
| PGDH.....           | Prostaglandin dehydrogenase                               |
| PGE2.....           | Prostaglandin E2                                          |
| PGF2 $\alpha$ ..... | Prostaglandin F2 $\alpha$                                 |
| PGs.....            | Prostaglandins                                            |
| phIGFBP.....        | Phosphorylated Insulin-like growth factor binding protein |
| PMN.....            | Polymorphonuclear cells                                   |
| PPROM.....          | Preterm premature rupture of membranes                    |
| PROM.....           | premature rupture of membranes                            |
| PTL.....            | Preterm labor                                             |
| PVH.....            | Periventricular hemorrhage                                |

|            |                                                  |
|------------|--------------------------------------------------|
| PVL.....   | Periventricular leukomalacia                     |
| RBC's..... | Red blood cells                                  |
| RCOG.....  | Royal College of Obstetricians and Gynecologists |
| RDS.....   | Respiratory distress syndrome                    |
| SC.....    | Subcutaneous                                     |
| SIDS.....  | Sudden infant death syndrome                     |
| TAT.....   | Thrombin-antithrombin III                        |
| TLR.....   | Toll-like receptors                              |
| TNF.....   | Tissue necrosis factor                           |
| TRH.....   | Thyrotropin releasing hormone                    |
| UAE.....   | Uterine artery embolization                      |
| US.....    | Ultrasound                                       |
| UTI.....   | Urinary tract infection                          |
| VLBW.....  | Very low birth weight                            |
| WBC's..... | White blood cells                                |
| WHO.....   | World health organization                        |
| ZAM.....   | Zone of altered morphology                       |

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# Introduction & Aim of the Work

## INTRODUCTION

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Despite recent progress in perinatal medicine, preterm labor, defined as labor that occurs before completion of 37 weeks of gestation, remains one of the most serious problems facing obstetricians (**ACOG, 1995**).

It's estimated that the preterm delivery contributes to 70% of perinatal morbidity and mortality excluding those related to congenital malformations (**Challis, 2000**).

The incidence of preterm birth has risen over the past 20 years (**Joseph et al., 1998**).

Spontaneous preterm labor can be understood as a syndrome with a number of underlying causes including infection, maternal stress, uterine distention, placental hypoxia, bleeding and lack of prostaglandin dehydrogenase (**Hagberg and Wennerholm, 2000**).

It has been estimated that about 1/3 of preterm labor with intact membranes may be caused by intrauterine infection (**Cunningham et al., 2001**).

The risk for spontaneous preterm birth among women with bacterial vaginosis was doubled, although the samples were obtained early in pregnancy (**Jacobsson et al., 2002**).

Genitourinary chlamydial infection at 24 weeks' gestation was associated with two fold increase in spontaneous preterm birth (**Andrews et al., 2000**).

Quantitative ultrasound gray level analysis and tissue characterization of cervix predicts premature delivery and

provides additional information in the prediction of potential premature delivery (**Tekesin et al., 2003**).

Assessment of cervical length at 15 and 24 weeks' gestation is excellent to predict spontaneous preterm labor prior to 30 weeks (**Guzman et al., 2001**).

Cervicovaginal fetal fibronectin test is most accurate in predicting spontaneous preterm birth within 7-10 days of testing among women with symptoms of threatened preterm birth before advanced cervical dilatation (**Honest et al., 2002**).

Human chorionic gonadotropin (hCG) detected in cervicovaginal secretions of patients with symptoms suggestive of preterm labor is a predictor of preterm birth (**Sanchez-Ramos group, 2003**).

Detection of phosphorylated insulin- like growth factor binding protein -1 (IGFBP-1) in cervical secretion is a rapid and easily applicable test that highly anticipates preterm delivery in patients at risk (**Lembet et al., 2002**).

Measurement of uterine contraction frequency has been employed as a screening test to identify women with increased risk of preterm birth and as an aid in the early diagnosis of preterm labor (**Iams, 2003**).

To document preterm labor, there should be contractions occurring at the frequency of 4 in 20 minutes or 8 in 60 minutes plus progressive change in the cervix, dilatation greater than 1 cm or cervical effacement of 80% or greater (**ACOG, 1997**).

Administration of corticosteroids to the mother has been shown to be of great benefit to the survival of the preterm baby (**Crowley, 2002**).

The UK ORACLE II study found no evidence of benefit for the use of antibiotics in uncomplicated preterm labor (**Kenyon et al., 2001**).

Preterm birth is significantly reduced in women who received cerclage after developing ultrasound evidence of cervical shortening (**Althuisius et al., 2000**).

Treatment of preterm labor consists of bed rest, hydration, pharmacologic interventions and combination of these (**Nancy et al., 2003**).

The aim of tocolysis is to delay preterm delivery to allow time for maternal administration of corticosteroids and in-utero transfer to a tertiary perinatal centre, thereby reducing neonatal morbidity and mortality (**Duley, 2001**).

It has recommended that tocolysis are used in the presence of regular uterine contractions plus documented cervical changes or appreciable cervical dilatation or effacement (**ACOG, 1998b**).

Management of uterine contractions with first line tocolytic therapy can prolong gestation. Among the tocolytics, however,  $\beta$ -mimetics appear not to be better than other drugs and pose significant potential harms for mothers. Continued maintenance tocolytic therapy has little or no value (**Nancy et al., 2003**).

Calcium channel blockers appear to be preferable to beta mimetics, not only in reducing the number of preterm deliveries within seven days, but also because of less discontinuation for adverse drug reactions (*King et al., 2003*).

Oxytocin antagonists (Atosiban) appear to be as effective as  $\beta$ -mimetics. It has fewer maternal side effects but is much more expensive than other options in preterm labor (*Duley, 2001*).

The frequency of cesarean section continues to increase and parallels improvement in the survival rates of preterm infants. Today, about  $\frac{1}{3}$  of these infants are delivered by cesarean section mainly because of malpresentation or maternal complications, in conjunction with an unfavorable cervix (*Westgren, 1997*).

## **AIM OF THE WORK**

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The aim of this work is a systematic review of modern techniques in prediction of preterm labor and recent advances in management of preterm labor including new generations of tocolytic drugs.

# Review of Literature

## Chapter 1