

**UMBILICAL CORD SERUM AND  
MATERNAL SERUM INSULIN LIKE  
GROWTH FACTOR I IN UNCOMPLICATED  
PREGNANCY AND IN PREGNANCY  
COMPLICATED BY PREECLAMPSIA**

*Thesis*

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### **List of Abbreviations**

|                        |                                                                                      |
|------------------------|--------------------------------------------------------------------------------------|
| AC.....                | Abdominal Circumference                                                              |
| AGA.....               | Appropriate for Gestational Age                                                      |
| ALS.....               | Acid Labile Subunit                                                                  |
| APGAR 1 min.....       | APGAR Scoring After 1 Minute (Appearance, Pulse, Grimace, Activity, and Respiration) |
| APGAR 5 min.....       | APGAR Scoring After 5 Minutes                                                        |
| BPD.....               | Bi-Parietal Diameter                                                                 |
| cFn.....               | Cellular Fibronectin                                                                 |
| CSF.....               | Cerebrospinal Fluid                                                                  |
| CVD.....               | Cardiovascular Disease                                                               |
| DBP.....               | Diastolic Blood Pressure                                                             |
| EPH-gestosis.....      | Edema, Proteinuria and Hypertension                                                  |
| FL.....                | Femur Length                                                                         |
| Fn.....                | Fibronectin                                                                          |
| HC.....                | Head Circumference                                                                   |
| hCG.....               | Human Chorionic Gonadotrophin                                                        |
| hGH.....               | Human Growth Hormone                                                                 |
| IGFs.....              | Insulin-Like Growth Factors                                                          |
| IGF-I.....             | Insulin-Like Growth Factor-I                                                         |
| IGF-II.....            | Insulin-Like Growth Factor-II                                                        |
| IGFBPs.....            | Insulin-Like Growth Factors Binding Proteins                                         |
| IL-6.....              | Interleukin-6                                                                        |
| IUGR.....              | Intrauterine Growth Retardation                                                      |
| KD.....                | Kilo Dalton                                                                          |
| MSA.....               | Multiplication Stimulating Activity                                                  |
| MSAFP.....             | Maternal Serum A-Fetoprotein                                                         |
| M W.....               | Molecular Weight                                                                     |
| NKB.....               | Neurokinin B                                                                         |
| NSILA.....             | Non-Suppressible Insulin Like Activities                                             |
| ng /ml.....            | Nanogram/Ml                                                                          |
| OGTT.....              | Oral Glucose Tolerance Test                                                          |
| PDE5.....              | Phosphodiesterase 5                                                                  |
| PE.....                | Pre-Eclampsia                                                                        |
| PGI <sub>2</sub> ..... | Prostacyclin                                                                         |
| PIH.....               | Pregnancy Induced Hypertension                                                       |
| PlGF.....              | Placental Growth Factor                                                              |
| Roc curve.....         | Receiver Operator Characteristic Curve                                               |

*Continued*

|                        |                                    |
|------------------------|------------------------------------|
| sFlt1.....             | Soluble fms-Like Tyrosine Kinase   |
| SGA.....               | Small for Gestational Age          |
| SBP.....               | Systolic Blood Pressure            |
| SHBG.....              | Sex Hormone Binding Globulin       |
| Sms.....               | Somatomedins                       |
| SmA.....               | Somatomedin A                      |
| SmB.....               | Somatomedin B                      |
| SmC.....               | Somatomedin C                      |
| TNF- $\alpha$ .....    | Tumor Necrosis Factor-Alpha        |
| TxA <sub>2</sub> ..... | Thromboxane                        |
| VEGF.....              | Vascular Endothelial Growth Factor |

# Introduction

## INTRODUCTION

---

Preeclampsia is a disorder that is believed to affect to some degree 1 in 10 of all pregnancies. It is the commonest single cause of maternal and fetal mortality, and currently there is no cure other than termination of the pregnancy (**Roberts and Redman, 1993**). The causes of preeclampsia are complex and not fully understood, but the condition may be associated with poor placentation (**Brosens et al., 1972**).

It is assumed that poor placentation and the associated obstructive lesion of the spiral arteries called acute atherosclerosis, lead to placental ischemia (**Redman and Sargent, 2000**). It is possible that preeclampsia causes placental ischemia, although it is more likely that placental ischemia causes preeclampsia especially because poor placentation is an early preclinical development (**Combs et al., 1993**).

It is presumed that blood born agents arising from the ischemic placenta are the cause of the generalized endothelial cell damage that gives rise to the preeclampsia syndrome (**Roberts et al., 1989**).

Preeclampsia is characterized by hypertension, proteinuria and edema which remits after delivery (**Dekker and Sibai, 1991**). Many lines of evidence point to an important role for the insulin-like growth factors (IGFs) in embryonic and fetal growth in human pregnancy (**Jones and Clemmons, 1995**) and during preeclampsia maternal serum IGF-I concentrations are lower than those in normal pregnant women (**Halhali et al., 1995 & Giudice et al., 1997**). The actions of IGFs are modulated by a series of at least six high affinity-

binding proteins, named as IGF binding proteins that are ubiquitously expressed. The role of these IGFBPs in IGF action is not clear, but it has been demonstrated that these proteins may enhance or inhibit IGF-cellular effects (**Rosenfeld et al., 1999**). In the circulation, IGFBP-3 is the major carrier protein for IGF-I and IGF-II; approximately 95% of IGF-I is bound to IGFBP-3 (**Binoux and Hossenlopp, 1988**). In a study done by **Wang et al. (1996)** decreased serum IGFBP-3 levels were observed in preeclamptic women, but in another study, this protein was not significantly decreased in preeclamptic patients (**Giudice et al., 1997; Varma et al., 1993**).

In normal pregnancy, maternal serum levels of IGF-I decrease early but increase again from gestational week 22 onward. Maternal IGF-I is believed to originate mainly from the maternal liver, and human growth hormone has been suggested to be a main stimulator of its synthesis (**Wang et al., 1996**). Preeclampsia is also associated with reduced utero--placental blood flow and fetal intrauterine growth retardation (**National High Blood Pressure Education program working group, 1990; Redman, 1991**). Insulin-like growth factor-I (IGF-I) may be involved in both normal and abnormal fetal growth (**Chard, 1994**).

Under physiological conditions, approximately 75% of IGF-I circulate as a high molecular mass (150-kDa) ternary complex formed by IGF-I, IGFBP-3 and an acid-labile subunit; 24% is bound to other IGFBPs, and the remaining 1% circulates as free IGF-I (**Rajaram et al., 1997**).