

Association between Serum Concentration of Free Testosterone and Pre-eclampsia

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(... رَبِّ أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ
الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَى وَالِدَيَّ
وَأَنْ أَعْمَلَ صَالِحاً تَرْضَاهُ وَأَدْخِلْنِي
بِرَحْمَتِكَ فِي عِبَادِكَ الصَّالِحِينَ)

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List of Abbreviations

<i>Abbrev.</i>	<i>Full term</i>
ALT	: Alanine aminotransferase
AST	: Aspartate aminotransaminase
BP	: Blood pressure
DCs	: Dendritic cells
H/R	: Hypoxia-reoxygenation
HLA-G	: Human leukocyte antigen
KIRs	: Killer immunoglobulin receptors
LDH	: Lactate dehydrogenase
LH	: Lutenizing hormone
Mg	: Milligram
MMPs	: Matrix metalloproteinases
NK	: Natural killer
PECAM	: Platelet endothelial cell adhesion molecule-1
PIH	: Pregnancy-induced hypertension
sEng	: soluble endoglin (sEng)
SHRG	: Serum sex hormone binding globulin
SPSS	: Statistical package for social sciences
TGF	: Transforming growth factor
uNK	: Uterine Natural killer
VCAM-1	: Vascular cell adhesion molecule-1

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Introduction

Preeclampsia is a transient but potentially dangerous complication of pregnancy that affects three to five percent of pregnant women (*Skjaerven et al., 2002*).

Preeclampsia is a disease unique to human pregnancy characterized by hypertension, proteinuria and edema due to fluid retention developing after twenty weeks gestational age (*Pipkin, 2001*).

Preeclampsia with its complications such as prematurity, IUGR, perinatal asphyxia and abruptio placentae is one of major causes of maternal and fetal morbidity and mortality due to its morbid course so it is necessary to identify those at risk for the illness and take precautions (*Gerulewicz-Vannini et al., 2006*).

In spite of so many researches, the pathology of preeclampsia has not been fully elucidated. Hormonal features of this condition have lead to speculation about hormonal causes

The lack of knowledge about the etiology makes it difficult to assess the risk factors (*Ficiologlu and Kutlu, 2003*).

Hyperandrogenism may be implicated in the pathogenesis of preeclampsia. It is hypothesized that there may be difference between the level of testosterone in pregnant women complicated with preeclampsia and those of matched women without this complication (*Ghorashi and Sheikhvatan, 2008*).

The study of blood testosterone may be implicated in pathogenesis of preeclampsia. Testosterone is produced in female ovaries and adrenal gland. Depending on the tissues, testosterone can be further converted to dihydrotestosterone and estradiol (***Ghorashi and Sheikhvatan, 2008***).

The serum testosterone concentration increases progressively throughout pregnancy, an effect that is due primarily to a progressive estrogen-induced increase in serum sex hormone-binding globulin (SHBG) concentrations. The increase in testosterone concentration in normal pregnancies occurs as early as 15 days after the LH surge, implying luteal phase ovarian production rather than adrenal production (***Laivuori et al., 1998***).

Aim of the Work

The aim of this work is to evaluate the level of testosterone in pregnant women with preeclampsia in the third trimester to find out the possible relation between the level of free serum testosterone and occurrence of preeclampsia.

Terminology and Classification

Preeclampsia is a disorder unique to human pregnancy characterized by a generalized systemic maternal inflammatory response, associated with diffuse endothelial cell dysfunction. It is one of the leading causes of maternal and perinatal morbidity and mortality, affecting 5% to 7% of all pregnancies, yet the etiology and pathogenesis have not been fully defined (*Tang et al., 2009*).

The term gestational hypertension is used now to describe any form of new onset pregnancy related hypertension.

The national high blood pressure education program's working group on high blood pressure in pregnancy recently issued a report proposing the classification of hypertension in pregnancy is related to one of four conditions:

- 1) Chronic hypertension that predate pregnancy.
- 2) Pre-eclampsia-eclampsia (a serous systemic syndrome of elevated blood pressure, proteinuria and other findings).
- 3) Chronic hypertension with super-imposed pre-eclampsia.
- 4) Gestational hypertension or non-proteinuric hypertension of pregnancy.

(Marik, 2009)

Table (1): Classification of hypertension in pregnancy

➤ Chronic hypertension ▪ BP> 140 mmHg systolic or 90 mmHg diastolic prior to pregnancy or before 20 weeks gestation ▪ Persists > 12 weeks postpartum ➤ Preeclampsia ▪ BP>140 mmHg systolic or 90 mmHg diastolic with proteinuria (>300 mg/24 hrs) after 20 weeks gestation ▪ Can progress to eclampsia (seizures) ▪ More common in nulliparous women, multiple gestation, women with hypertension for >4 years, family history of preeclampsia, hypertension in previous pregnancy, renal disease ➤ Chronic hypertension with superimposed preeclampsia ▪ New onset proteinuria after 20 weeks in a woman with hypertension ▪ In a woman with hypertension and proteinuria prior to 20 weeks gestation ▪ Sudden two- to threefold increase in proteinuria ▪ Sudden increase in BP ▪ Thrombocytopenia ▪ Elevated AST or ALT ➤ Gestational hypertension ▪ Hypertension without proteinuria occurring after 20 weeks gestation ▪ Temporary diagnosis ▪ May represent preproteinuric phase of preeclampsia or recurrence of chronic hypertension abated in midpregnancy ▪ May evolve to preeclampsia ▪ If severe, may result in higher rates of premature delivery and growth retardation than mild preeclampsia ➤ Transient hypertension ▪ Retrospective diagnosis ▪ BP normal by 12 weeks postpartum ▪ May recur in subsequent pregnancies ▪ Predictive of future primary hypertension

ALT, alanine aminotransferase; AST, aspartate aminotransaminase;
BP, blood pressure

(Marik, 2009)

Table (2): Diagnosis of hypertensive disorders complicating pregnancy

Gestational hypertension:

BP >140/90mmHg for first time during pregnancy No proteinuria.
BP returns to normal <12 weeks' postpartum.
Final diagnosis made only postpartum.
May have other signs or symptoms of pre-eclampsia, for example, epigastric discomfort, or thrombocytopenia.

Pre-eclampsia

Minimum criteria

BP >140/90mmHg after 20 weeks' gestation.
Proteinuria >300mg/24hrs of >1+ dipstick

Increased certainty of pre-eclampsia:

BP >160/110mmHg.
Proteinuria 2.0g/24hrs or >2+ dipstick.
Serum creatinine >1.2mg/dL unless known to be previously elevated.
Platelet <100.000/mm³.
Microangiopathic hemolysis (increased LDH).
Elevated ALT or AST.
Persistent headache or other cerebral or visual disturbance.
Persistent epigastric pain.

Eclampsia:

Seizure that cannot be attributed to other causes in a women with pre-eclampsia.

Superimposed pre-eclampsia (on chronic hypertension)

New-onset proteinuria >300mg/24hrs in hypertensive women but no proteinuria before 20 weeks' gestation.
A sudden increase in proteinuria or blood pressure, platelet count <100.000/mm³ in women with hypertension and proteinuria before 20 weeks' gestation.

Chronic hypertension:

BP >140/90mmHg before pregnancy or diagnosed before 20 weeks' gestation not attributed to gestational trophoblastic disease.

Or

Hypertension first diagnosed after 20 weeks' gestation and persistent after 12 weeks' postpartum.

ALT= alanine aminotransferase; AST= aspartate aminotransferase;
BP= blood pressure; LDH= lactate dehydrogenase.

(Marik, 2009)