SERUM CONCENTRATIONS OF CA-125 IN NORMAL AND PREECLAMPTIC PREGNANCIES

Thesis

Submitted for the Partial fulfillment of Master Degree
in Obstetrics and Gynecology

Presented By

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2014

Acknowledgement

No words can fulfill the feeling of gratitude and respect I carry for ***Professor Dr. Helmi Motawe El-Sayed*** for his patient guidance, enthusiastic encouragement and useful critiques of this research work.

I would like to express my great appreciation to ***Dr. Mohamed El-Mandooh Mohamed*** for his professional guidance, valuable support and useful and constructive recommendations on this project with a scientific personality and a kind heart.

I would like to express my deep gratitude and respect to ***Dr. Sherif Fathi El-Mekkawi*** for his valuable and constructive suggestions during the planning and development of this research work. His willingness to give his time so generously has been very much appreciated.

Finally, I wish to thank my family for their support and encouragement throughout my study.

Ahmed Aziz Brekaa

ABSTRACT

Aim: This prospective study aims to investigate the serum concentrations of CA-125 in normal and preeclamptic pregnancies and thus to specify the value of this biochemical marker in prediction and diagnosis of preeclampsia.

Methods: This study reviews a total of 72 primigravid women with singleton pregnancy. These participants were categorized into two groups: control (n = 36) and preeclampsia (n = 36).

Results: Serum CA-125 concentrations were found to correlate positively with diastolic blood pressure (r = 0.345, P-value < 0.001) and maternal age (r = 0.052, P-value = 0.002) but no significant correlation was found with systolic blood pressure, platelet count and gestational age at time of delivery. When the cut-off point for serum CA-125 concentration was accepted as 51.38 IU/ml, the sensitivity and specificity of this biochemical marker were, respectively, 63.9% and 97.2% for the detection of preeclamptic pregnancies. On the other hand, positive and negative predictive values for CA-125 were 95.8% and 72.9%, respectively.

Conclusion: This study suggests that CA-125 is a biochemical marker which reflects the underlying inflammatory process in preeclampsia.

Keywords: CA-125 – Preeclampsia – Pregnancy

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LIST OF ABBREVIATIONS

Aa .....Acute atherosis

ACOG .....American College of Obstetricians and Gynecologists

Ang-1 .....Angiopoietin-1

Ang-2 .....Angiopoietin-2

Ang-II .....Angiotensin II

AT1-AA .....Angiotensin II type 1 receptor autoantibody

AT1-AB .....Angiotensin II type 1 receptor antibody

$BKCa^{++}$ .....Large conductance calcium-activated potassium channels

BMI .....Body mass index

BP .....Blood pressure

CA-125 .....Cancer Antigen-125

CO .....Carbon monoxide

CRP .....C-reactive protein

CT .....Computed Tomography

DIC .....Disseminated intravascular coagulation

ET-1 .....Endothelin-1

ffDNA .....Free fetal DNA

FSH .....Follicle stimulating hormone

GAWS .....Genome-wide association screening

GFR .....Glomerular filtration rate

GWLS .....Genome-wide linkage analyses

hCG .....Human chorionic gonadotropin

hCG-h .....Hyperglycosylated human chorionic gonadotropin

hCG-α .....Alpha subunit of human chorionic gonadotropin

hCG-β ..... Beta subunit of human chorionic gonadotropin

HELLP ..... Hemolysis, elevated liver enzymes, low platelet count

HO-1 ..... Heme oxygenase-1 system

IBI ..... Inter-birth interval

IGF ..... Insulin-like growth factor

IGFBP ..... Insulin-like growth factor binding protein

IL ..... Interleukin

IUFD ..... Intrauterine fetal demise

IUGR ..... Intrauterine growth restriction

kDa ..... Kilodalton

LH ..... Luteinizing hormone

MELD ..... Model for End-Stage Liver Disease

MRI ..... Magnetic resonance image

NO ..... Nitric oxide

OR ..... Odds Ratio

PAI-1 ..... Plasminogen activator inhibitor-type 1

PAPP-A ..... Pregnancy-associated plasma protein-A

PCR ..... Polymerase chain reaction

PE ..... Preeclampsia

PI ..... Pulsatility index

PlGF ..... Placental growth factor

RBF ..... Renal blood flow

RI ..... Resistive index

ROS ..... Reactive oxygen species

RR ..... Risk Ratio

RUPP ..... Reduced uterine perfusion pressure

Siglec-9 ..... Sialic acid-binding Ig-like lectin-9

sFlt-1 ..... Soluble fms-like tyrosine kinase-1

SRD ..... Serous retinal detachment

sTie-2 ..... Soluble endothelial cell-specific tyrosine kinase receptor-2

STOX-1 ..... Storkhead box-1

sVEGFR-1 ... Soluble vascular endothelial growth factor receptor-1

TNF ..... Tumor necrosis factor

TSH ..... Thyroid stimulating hormone

VEGF ..... Vascular endothelial growth factor

WHO ..... World Health Organization

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Introduction

Preeclampsia complicates 3–5% of all pregnancies in the world. It is associated with hypertension and proteinuria existing after the 20th week of pregnancy. Many risk factors such as primigravida, younger age and twin pregnancy have been identified. The main consequence of placental ischemia is the generalized endothelial dysfunction, which is responsible for clinical symptoms and complications (e.g. eclampsia, placental abruption and HELLP syndrome) ***(Cisse et al., 2004).***

The diagnosis of gestational hypertension is made when blood pressure reaches 140/90 mmHg or greater for the first time after mid-pregnancy in absence of proteinuria. Almost half of these women subsequently develop preeclampsia syndrome, which includes signs such as proteinuria and thrombocytopenia or symptoms such as headaches or epigastric pain. Gestational hypertension is reclassified as transient hypertension if evidence for preeclampsia does not develop, and the blood pressure returns to normal by 12 weeks postpartum ***(Chesley, 1985).***

Proteinuria is the surrogate marker that defines the endothelial leak which characterizes the preeclampsia. Even so, when blood pressure increases, it’s dangerous to both mother & fetus to ignore this sign because proteinuria

has not yet developed. It is important to know that 10% of eclamptic seizures develop before overt proteinuria is identified ***(Chesley, 1985).***

Proteinuria is defined by 24 hour urinary protein excretion exceeding 300 mg, a urine protein/creatinine ratio of 0.3, or persistent 30 mg/dL (1+ dipstick) protein in random urine samples ***(Lindheimer et al., 2008).***

CA-125 (Cancer Antigen-125 or Carbohydrate Antigen-125) is a large molecule mostly consisting of highly glycosylated glycoproteins. It is exposed in amnion & its derivatives of fetal coelomic epithelia (as Mullerian epithelia, peritoneum, pleura and pericardium) & in many adult tissues (as epithelium of the fallopian tubes, endometrium, endocervix, pleura and peritoneum) ***(Kabawat et al. 1983).***

The normal endometrium produces CA-125 and this production can contribute significantly to the level of circulating CA-125 at the time of menstruation. During peritoneal irritation (ovarian hyperstimulation syndrome, salpingitis, ruptured ectopic pregnancy and laparotomy), peritoneally derived CA-125 significantly contributes to circulating CA-125 concentrations, giving elevated CA-125 values ***(Bischof et al., 1986).***

In pregnant women, the CA-125 levels are increased reaching highest levels during the first trimester. The values typically decrease during the late first trimester and should remain below 35 IU/ml of serum until delivery. In some instances the maternal serum CA-125 remains within normal values (0-35 IU/ml) throughout uncomplicated pregnancies ***(Kenemans et al., 1993).***