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مقدمة من

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٢٠١٢

THE RATIO OF T-HELPER TYPE-1: T-HELPER TYPE-2 IMMUNITIES IN CORRELATION WITH DOPPLER BLOOD FLOW VELOCIMETRY IN E.P.H.GESTOSIS

Thesis

Submitted for partial fulfillment of MD degree in Obstetrics & Gynecology

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بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ
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وَكَانَ فَضْلُ
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List of Abbreviations

Abbrev.	Meaning
ABC	Airway, breathing and circulation
AFI	Amniotic fluid index
ASA	Acetylsalicylic acid
AT1-AA	Agonistic autoantibodies to the angiotensin II type I receptor
BP	Blood pressure
Bpp	Biophysical profile
CBC	Complete blood count
CNS	Central Nervous System
DBP	Diastolic blood pressure
ELISPOT	Enzyme-linked immunosobent spot assay
EPH Gestosis	Edema proteinuria hypertension gestosis
FOX P3	Forkhead box protein
HELLP	Hemolysis Elevated Liver enzymes Low Platelet count
20-HETE	20-Hydroxyeicosatetraenoic acid
HLA	Human leucocyte antigen
IFN--γ	Interferon gamma
IL-2	Interleukin 2
IV	Intravenous
LDH	Lactate dehydrogenase
LFTs	Liver function tests
mmHg	Millimeter mercury
MMP-2	Matrix metalloproteinase-2
NK T cells	Natural killer T cells
uNK	Uterine natural killer
NO	Nitric Oxide
NST	Non Stress Test

INTRODUCTION

E.P.H. Gestosis complicates up to 10% of all pregnancies and is associated with increased risk of adverse fetal, neonatal and maternal outcomes, including preterm birth, intrauterine growth restriction, perinatal death, acute renal or hepatic failure, ante partum haemorrhage, post partum hemorrhage and maternal death ***(Duley, 2009 and Steegers et al., 2010).***

Risk factors for E.P.H. Gestosis have been well documented ***(Lawler et al., 2007).*** Factors that increase risk include multiparity, older maternal age, multiple births, diabetes, chronic hypertension, obesity, previous E.P.H. Gestosis, family history of E.P.H. Gestosis, a new partner and/or ≥10years since last pregnancy, renal disease and or the presence of antiphospholipids antibodies ***(Roberts et al., 2005 and Steegers et al., 2010).***

Decreased risk of E.P.H. Gestosis has been associated with placenta praevia, smoking, summer births, low dose aspirin and calcium supplementation in high risk women, treatment of gestational diabetes and use of antihypertensive medications ***(Algert et al., 2010; Ness et al., 2008 and Steegers et al., 2010).***

Etiology of E.P.H Gestosis has been ascribed to generalized maternal endothelial cell dysfunction ***(Roberts***

et al., 1999), poor trophoblastic implantation ***(Pijnenborg 1996 and Zhou et al., 1997)*** and excessive inflammatory response ***(Redman et al., 1999).***

The diagnosis of E.P.H Gestosis can have serious implications for mother &fetus. E.P.H Gestosis account for 15% of preterm birth and their associated morbidities and mortalities ***(Meis et al., 1998),*** and can also lead to intrauterine growth restriction and death ***(Solomon et al., 2004).***

Maternal complications include an increased risk of stroke and circulatory collapse ***(Chesley 1984).***

Careful management has led to a decrease in maternal mortality resulting from E.P.H Gestosis in developed countries ***(Walker, 2000),*** however the associated maternal mortality rate in developing world remains high ***(Dueley, 1992).***

Lymphocyte is a small cell found in blood, from which it re circulate through the tissues and back via the lymph, “policing” the body for non self material. Its ability to recognize individual antigens through its specialized surface receptors and to divide into numerous cells of identical specificity and long lifespan makes it the ideal cell for adaptive responses. Two major populations of lymphocytes are recognized: T and B-lymphocytes secrete

antibodies, the humoral element of adaptive immunity. T "thymus derived" lymphocytes are further divided into subpopulations which "help" B lymphocytes, kill virus infected cells, activate macrophages, etc ***(Playfair and Chain, 2001).***

T cells can be classified as T helper 1 (Th1) cells, which synthesize interleukin 2 (IL-2), interferon-γ (IFN-γ) , and tumor necrosis factor –β (TNF-β), and induce cellular immunity, or T helper 2 (Th2) cells which synthesize IL-4,IL-5, IL-6, IL-10 and IL-13 and induce antibody production ***(Mosmann et al., 1996).***

There are different reports indicating that, in normal pregnant women production of Th2 cell-derived cytokines by peripheral blood mononuclear cells is increased and that of Th1 cell-derived cytokines is decreased ***(Marzi et al., 1996).***

On the other hand, there were various reports demonstrating that in normal pregnant women both circulating IFN-γ produced by Th1 cells and IL-4, one of Th2 cells are increased ***(Matthiesen et al., 1998).***

Up-regulation of Th1 responses occurs not only in peripheral blood also at the feto maternal interface in patients with E.P.H .Gestosis ***(Saito et al., 1999b; Rein et al., 2002 and Sakai et al., 2002).***

In patients with E. P. H. Gestosis, the T-cell activation marker HLA-DR is extremely high expressed on CD8-positive T cells ***(Saito et al., 1999b).***

Nebelhut et al. (1992), have reported that E. P. H. Gestosis is associated with increases in soluble IL-2 receptor and in soluble CD8 concentrations that reflect the severity of hypertensive disorder.

The developed technique of flow cytometry for intracellular cytokines is very useful. Some reports that Th1 (CD4+IL4+IFN-γ) cells are decreased in E.P.H Gestosis ***(Saito et al., 1999c).***

Doppler ultrasound has been used in almost every medical discipline to study blood flow in diseases where an alteration of this dynamic system in anticipated. The first Doppler ultrasound report using continuous wave assessment of umbilical artery flow was published in 1977 ***(Fitzgerald, 1977).***

The relationship between abnormal uterine artery Doppler velocimetry and E.P.H Gestosis, intrauterine growth retardation and adverse pregnancy outcome is well established ***(Aquilina, 1996).***

Doppler ultrasound of the umbilical artery is more helpful than other tests of fetal wellbeing ***(Harmann, 2003).***

The effects of Doppler Ultrasound in high risk pregnancies in obstetrical care and fetal outcomes were systematically reviewed ***(Neilson, 2003).*** The use of Doppler in pregnancies complicated by hypertension or presumed impaired fetal growth was associated with a trend in reduction of peri natal death.