CHANGES OF INTERLEUKIN-٦ IN PATIENT OF SEVER PREECLAMPSIA BEFORE AND AFTER TERMINATION

Thesis

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Lists of Abbreviations

١st	First……
٢nd	Second……
<	Less than……
>	More than……
α	Alpha……..
γ	Gama……..
Ang	Angioprotiens gene……
APLABS	Auto immune phospholipids antibodies…….
ALT	Alanin transferase……
AST	Aspartate transferase……
B	Beta…….
Bp	Bood pressure…….
BMI	Body mass index……..
CBC	Complete blood count……
Cm	Centimter……
CS	Cesarean section…….
CT	Coputerized tomography……
DOC	Deoxycorticosterone……..
DM	Diabetes mellitus…….

F.H.S	Fetal heart sound……..
FFAs	Free fatty acids …….
HIF-١ α	Hypoxia-inducible factor-١……...
Hr	Hour……..
Il-٦	Interleukin-٦……
IL-٨	Interleukin-٨……
IL-١ β	Interleukin-١ beta……
I/R	ischaemia–reperfusion……..
IV	Intravenous……
IU	International unit……..
Kg	Kilogram……
Mcg	Microgram…….
Mg	Milligram……
ML	Milliletre……
Mm	Millimeter……..
NO	Nitous oxide……..
OFR	$O_٢$ free radicals…….
PG ١٢	Prostaglandine ١٢
PIGF	placental growth factor……..
PROM	Premature rupture of membrane……

RAS	Renin angiotensin system…….
SLE	Systemic lupus erythromatosis……..
TGF-٣ β	Transforming growth factor beta ٣……
TNF-α	Tumor necrosing factor alpha……..
Th	T- helper……
Th١	T- helper type ١…….
Th٢	T- helper type ٢……
US	Ultra sound……
U/L	Unit per litre……...
VD	Vaginal delivery…….
VEGF	Vascular endothelial growth factor……
WHO	World Health Organization……..

Introduction

Pre-eclampsia is a hypertensive and multiple system disorder unique to human pregnancy. Although the etiology of pre-eclampsia remains unknown, there are many proposed theories regarding the pathogenesis of the pre-eclamptic disease processes as: oxidative stress; abnormal trophoblast invasion; vascular endothelial dysfunction; genetic predisposition; dietary deficiencies; and defective immunological adaptation to pregnancy **(David et al., ٢٠٠٩).**

Pre-eclampsia is one of the most recognized clinical causes of high-risk pregnancies. Although pre-eclampsia affects about ١٪–٢٪ of pregnancies in some European countries, its prevalence can be up to ١٠٪–١٥٪ in some South American and African countries **(Sucak et al., ٢٠١٠).**

Pre-eclampsia has a greater genetic component determined by multiple genes, the number of genes involved in the susceptibility to develop pre-eclampsia increases rapidly. Nearly ٥٠ maternal genes have been analyzed; most of these studies have been approaches to identify a genetic association, comparing the frequencies of genetic polymorphisms between cases and controls **(Norma, ٢٠٠٦).**

Conditions associated with oxidative stress, include, obesity, chronic hypertension and diabetes, where antioxidant reserves may be inadequate. These observations have led to trials of prophylactic effects of antioxidants, including Vitamins C and E and Selenium. A recent Cochrane review of seven randomized trials reported a ٣٩٪reduction in the risk of pre-eclampsia associated with oral antioxidant supplements **(Sally and Linda, ٢٠٠٦).**

A shallow trophoblast invasion is one of the mechanisms strongly affiliated to the pathogenesis of pre-eclampsia. It is claimed that shallow trophoblastic invasion might lead to poor placental vascularization that will result in both deficient anchoring in the matrix tissue and placental ischemia ending in the release of inflammatory cytokines in maternal circulation starting the process of pre-eclampsia **(Leif et al., ٢٠٠٥).**

The increased syncytiotrophoblast deportation in pre-eclampsia is probably explained by the presence syncytial sprouts that may be elongated on long pedicles. Cytotrophoblast proliferation and formation of these outgrowth lesions of syncytiotrophoblast may represent evidence of placental repair mechanisms. Pre-eclampsia is associated with glycogen accumulation in syncytiotrophoblast, which could be another expression of increased syncytiotrophblast deportation and increased cytotrophoblast proliferation **(Gustaaf et al., ١٩٩٨).**

Dys-regulation of the maternal immune response towards the fetus might be the causal factor of shallow trophoblastic invasion **(Reza et al., ٢٠٠٧).**

It has been proved that in pre-eclamptic patients, there is up-regulation of Th١ activity with the abnormal release of increasing amounts of pro-inflammatory cytokines as IL-١٢ and TNF-α **(Jacek et al., ٢٠٠٢).**

And these pro-inflammatory cytokines might be the causal factor of generalized endothelial dysfunction that is characteristic to pre-eclampsia **(Reza et al., ٢٠٠٧).**

Inflammatory cytokines are known to be potent activators of vascular endothelial and have been proposed as mediators of endothelial dysfunction during pre-eclampsia **(Sazina et al., ٢٠٠٣).**

In normal pregnancy, particularly, at the maternal-fetal interface, anti-inflammatory cytokines produced by T helper (TH٢) cells predominate, regulating trophoblast cell growth, differentiation and invasion for embryo implantation and therefore, an appropriate balance between pro-(TH١) and anti (TH٢) inflammatory cytokines is thought to be crucial for determining the success or failure of pregnancy. Endothelial dysfunction, present in pre-eclamsia, may cause abnormal immune (TH١) activation, causing disturbed balance between pro-inflammatory (tumor factor necrosis-α (TNF-A), interleukin (IL)-٦, IL-٢, IL-١β) and anti-inflammatory (IL-٤,

IL-١٠, IL-١٣) cytokines, which compromises uteroplacental perfusion and perpetuates further vascular damage (**Archana et al., ٢٠١٠).**

Many pro-inflammatory cytokines and modulators are founded at increased levels in both circulation and placenta during pre-eclamptic pregnancy. Two of them tumor factor necrosis-α (TNF-α) and interleukin-١(IL-١) have both been implicated in pre-eclampsia pathophysiology, since they have the ability to stimulate structural and functional alternation in endothelial cells **(Hanna Peterson., ٢٠١٠).**

Interleukin-٦ is TH٢ cytokine and has been shown to induce lymphocyte proliferation, and T-cell, B-cell differentiation, and to stimulate hepatic acute phase proteins **(Robin, ٢٠٠٥).**

Cytokines known to play important role in maintenance Of normal pregnancy as well as development of pathological status. There is a hypothesis of altered immune response in preeclampsia and suggests that dysregulation of cytokine expression occurs in preeclampsia with increase levels of pro-inflammatory cytokines. Inadequate trophoblast invasion and failure of physiological remodeling of spiral arteries of placenta in preeclampsia stimulate over production of inflammatory Th١ cytokines (interleukin-٦) causing endothelial damage. Chronic infusion of interleukin-٦ into normal pregnancy rates has been

to significantly increase arterial pressure and impair renal hemodynamics.

There is a significant negative correlation was observed between levels of endothelial nitrous oxide and interleukin-٦(i.e. decrease endothelial nitrous oxide levels with increase interleukin-٦ levels.) which indicates that interleukin-٦ might be a possible mediator of increase vascular resistance during preeclampsia **(Archana, ٢٠١٠).**