

# **Clinical Significance of Plasma Levels of Pentraxin-3 in Pre-eclampsia Patients**

Thesis

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# الأهمية الإكلينيكية لنسبة البنتراكسين ٣ في البلازما لدى الحوامل المصابات بتسمم الحمل

رسالة

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في الباثولوجيا الإكلينيكية والكيمائية

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## SUMMARY AND CONCLUSION

Pre-eclampsia is a potentially serious condition that still accounts for significant morbidity and mortality for the mother and the neonate, complicating 5-7% of all pregnancies and exposing them to a 3- to 25-fold increased risk of severe obstetric complications. Although, the pathogenesis is not fully understood, it is now widely accepted that vascular endothelial dysfunction is the most astonishing and the principal event in the pathophysiology of the disease.

Researchers investigated the fact that endothelial dysfunction has been hypothesized to be part of an excessive maternal inflammatory response to pregnancy. Complement activation, activated circulating leukocytes, increased release of reactive oxygen species, and increased levels of various inflammatory cytokines in pre-eclampsia.

Pentraxin-3 (PTX-3) is a described inflammatory molecule that belongs to the well known CRP family. PTX-3 differs from CRP in terms of cellular origin, molecular inducers, and kinetics of production. It is expressed by different cells like endothelial cells, monocytes, macrophages, and fibroblasts exposed to inflammatory stimuli. PTX-3 plasma levels increase dramatically during endotoxic shock, sepsis, or other inflammatory conditions. Recent studies suggest that PTX-3 plays an important role in innate immunity, female fertility, and inflammatory processes, so this promoted us to investigate this molecule in pre-eclampsia.

In this regard, this study aimed to evaluate the clinical utility of pentraxin-3 in diagnosis of pre-eclampsia and assessment of severity of the disease in comparison to CRP. In addition, the role of PTX-3 and CRP in fetal growth was evaluated.

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## List of Abbreviations

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<b>ACE</b>	Angiotensin-converting enzyme
<b>ACOG</b>	American College of Obstetrics and Gynecology
<b>AM</b>	Adrenomedullin
<b>AMI</b>	Acute myocardial infarction
<b>AT1</b>	Angiotensin II receptor-1
<b>CBC</b>	Complete blood picture
<b>CKD</b>	Chronic Kidney Disease
<b>COC</b>	Cumulus oophorus cells in ovary
<b>CTBs</b>	Cytotrophoblasts
<b>DBP</b>	Diastolic blood pressure
<b>DCs</b>	Dendritic cells
<b>ELISA</b>	Enzyme linked immunosorbent assay
<b>eNOS</b>	Endothelial nitric oxide synthase
<b>ET-1</b>	Endothelin-1
<b>Flt-1</b>	Fms-like tyrosine kinase-1
<b>GA</b>	Gestational age
<b>HELLP</b>	Hemolysis, elevated liver enzymes and low platelets
<b>IFN-<math>\gamma</math></b>	Interferon-gamma
<b>IGF</b>	Insulin-like growth factor Pentraxin-3 (PTX3)
<b>IL-1</b>	Interleukin-1
<b>IL-10</b>	Interleukin-10
<b>IL-2</b>	Interleukin-2
<b>IUGR</b>	Intrauterine growth restriction
<b>KDa</b>	Kilo Dalton
<b>LPS</b>	Lipopolysaccharide
<b>MDL</b>	Minimum detectable limit
<b>MMPs</b>	Matrix metalloproteinases

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## List of Abbreviations

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<b>NK</b>	Natural killer cells
<b>NO</b>	Nitric oxide
<b>NOS</b>	Nitric oxide synthase
<b>NPTXI</b>	Neural pentraxin I
<b>NPTXII</b>	Neural pentraxin II
<b>NSCLC</b>	Non-small cell lung cancer
<b>OMPs</b>	Outer membrane proteins
<b>PAI-1</b>	Plasminogen activator inhibitor-1
<b>PAPP-A</b>	Pregnancy associated plasma protein A
<b>PCR</b>	Polymerase chain reaction
<b>PDGF</b>	Platelet derived growth factor
<b>PTX-3</b>	pentraxin-3
<b>PIGF</b>	Placental growth factor
<b>PMNs</b>	Polymorphonuclear
<b>PP-13</b>	Placental protein-13
<b>RAS</b>	Rennin angiotensin system
<b>ROS</b>	Reactive oxygen species
<b>RT-PCR</b>	Reverse transcriptase PCR
<b>SAP</b>	Serum amyloid P-component
<b>SBP</b>	Systolic blood pressure
<b>SCLC</b>	Small cell lung cancer
<b>sEng</b>	Soluble endoglin
<b>sFlt1</b>	Fms-like tyrosine kinase-1
<b>SSC</b>	Systemic sclerosis
<b>TGF-<math>\beta</math>1</b>	Transforming growth factor- $\beta$ 1
<b>TLR</b>	Toll-like receptor
<b>TNF-<math>\alpha</math></b>	Tumor necrosis factor -alpha
<b>VEGF</b>	Vascular endothelial growth factor

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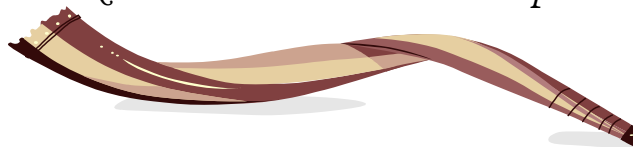
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## INTRODUCTION

Pre-eclampsia is a multisystem disorder specific to pregnant women. It remains one of the most important causes of maternal and fetal mortality and morbidity worldwide. It is the second largest cause of maternal mortality and affects 5% to 7% of pregnant women worldwide and approximately 3% of pregnant women in the western world (*Aida et al., 2009*). Pre-eclampsia is a major cause of preterm birth and intrauterine growth restriction accounting for 12-18% of pregnancy-related maternal deaths especially in developing countries (*Sharon et al., 2008*).

In spite of its relevant epidemiologic impact, the complete pathogenesis of this disease still remains unclear, underlining a multifactorial etiology. Deficient remodeling of the spiral arteries during the interaction between maternal and fetal sides at the time of trophoblast invasion has been postulated as a cause of placental insufficiency. This would lead to the release of inflammatory factors in the systemic maternal circulation (*Cetin et al., 2006*). Endothelial dysfunction has been hypothesized to be part of an excessive maternal inflammatory response to pregnancy. Complement activation, activated circulating leukocytes, increased release of reactive oxygen species, and increased levels of various inflammatory cytokines in pre-eclampsia all agree with this hypothesis (*Redman and Sargent, 2005*).

Several laboratory markers were found for detecting haemostatic system alterations in pregnancies complicated by pre-eclampsia. Among these are fibronectin which is related to blood pressure in pregnancy, in addition to serum amyloid A (SAA) and C-reactive protein (CRP) which are markers of tissue damage and inflammation (*Engin et al., 2007*).



Although these markers are altered in pre-eclampsia, they have a major disadvantage as they lack both specificity and sensitivity (*Baumann et al., 2010*).

Pentraxin-3 (PTX-3) is a described inflammatory molecule that belongs to the well known CRP family. PTX-3 differs from CRP in terms of cellular origin, molecular inducers, and kinetics of production. It is expressed by different cells like endothelial cells, monocytes, macrophages, and fibroblasts exposed to inflammatory stimuli (*Garlanda et al., 2007*). PTX-3 plasma levels increase dramatically during endotoxic shock, sepsis, or other inflammatory conditions. Recent studies suggest that PTX-3 plays an important role in innate immunity, female fertility, and inflammatory processes, so this promoted us to investigate this molecule in pre-eclampsia (*Souza et al., 2002*).



## **AIM OF THE WORK**

The aim of the present study is to assess the clinical utility of PTX3 as an early predictor of pre-eclampsia and assessment of its severity in comparison to CRP. In addition, the relation of PTX3 to fetal growth will be evaluated.