# CLINICAL UTILITY OF ADRENOMEDULLIN IN DIAGNOSIS OF PREECLAMPSIA

*Thesis*

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# Abbreviations

**Ab .....** Antibody

**AD.....** Alzheimer's disease

**ADH.....** Antidiuretic hormone

**Ag.....** Antigen

**ALT .....** Alanine aminotransferase

**AM.....** Adrenomedullin

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**AST.....** Aspartate aminotransferase

**ATPs.....** adenosine triphosphates

**AUC .....** Area under the curve

**bp .....** Base pair

**BUN .....** Blood urea nitrogen

**cAMP.....** 3', 5'-cyclic adenosine monophosphate

**CAP .....** Community-acquired pneumonia

**CBC .....** Complete blood count

**cDNA .....** Complementary DNA

**cGMP .....** Cyclic guanosine monophosphate

**CGRP .....** Calcitonin gene-related peptide

**CKD.....** Chronic kidney disease

**CLR .....** Calcitonin like receptor

**CNS .....** Central nervous system

**CRLR .....** Calcitonin-receptor–like receptor

**CSF .....** Cerebrospinal fluid

**CT .....** Computed tomography

**DIC .....** Disseminated intravascular coagulopathy

**DNA.....** Deoxy ribonucleic acid

**dsDNA .....** Double strand DNA

**dUTP .....** Deoxy uridine triphosphate

**EDTA .....** Ethylenediaminetetraacetic acid

**ELISA .....** Enzyme linked immunosorbent assay

**ESR.....** Erythrocyte sedimentation rate

**Ex .....** Exon

**FISH .....** Fluorescent insitu hybridization

**FN .....** False negative

**FP .....** False positive

**GA .....** Gestational age

**GBS .....** Group Bβ Streptococcus

**GFR .....** Glomerular filtration rate

**GIT .....** Gastrointestinal tract

**GM-CSF.....** Granulocyte-macrophage colony stimulating factor

**Hb .....** Hemoglobin

**HM.....** Hematologic malignancy

**HPA .....** Hypothalamo-pituitary-adrenal

**HPLC .....** High-performance liquid chromatography

**ID .....** Immune deficiency

**IEM .....** Inborn errors of metabolism

**IHC.....** Immunohistochemistry

**IQR.....** Interquartile range

**ISH.....** In situ hybridization

**mRNA .....** Messenger ribonucleic acid

**NO .....** Nitric oxide

**NPV .....** Negative predictive value

**NS .....** Neonatal sepsis

**OD .....** Optical denisty

**PAF.....** Platelet activating factor

**PAMP .....** Proadrenomedullin N-terminal 20 peptide

**PBS .....** Phosphate buffer saline

**PCR .....** Polymerase chain reaction

**PK.....** Protein kinase

**PKA .....** Protein kinase A

**PPV.....** Positive predictive value

**PRO-ADM .....** Pro-adrenomedullin

**PSI .....** Pneumonia Severity Index

**PTT.....** Activated partial thromboplastine time.

**RIA .....** Radio immunoassay

**ROC.....** Receiver-operating characteristic

**RT-PCR .....** Reverse transcription polymerase chain reaction

**SD .....** Standard deviation

**SIRS.....** Systemic inflammatory response syndrome

**TN.....** True negative

**TNF .....** Tumor necrosis factor

**TP .....** True positive

**UTIs .....** Urinary tract infections

**UV.....** Ultra violet

**VEGF .....** Vascular endothelial growth factor

**WBCs .....** White blood cells

**WHO .....** World Health Organization

**ZG.....** Zona glomerulosa

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# INTRODUCTION

Preeclampsia (PE) is a syndrome that embraces a wide spectrum of symptomatology. It's one of the leading causes of maternal morbidity and mortality. In recognition of the syndromic nature of PE, the American College of Obstetrics and Gynecology (ACOG) updated the definition of PE to be the presence of Maternal blood pressure ≥140/90 on two occasions at least 4 hours apart in a woman with a previously measured normal blood pressure, and proteinuria. Other signs and symptoms may also be present according to severity like thrombocytopenia <100,000 /µL, renal insufficiency, impaired liver function, pulmonary oedema or even cerebral or visual symptoms. In some cases PE can be asymptomatic and discovered upon a routine screening ***(ACOG, 2013).***

Preeclampsia causes remain unknown, and delivery remains the only definitive treatment. It is increasingly recognized that many pathophysiological processes contribute to this syndrome, with different signaling pathways converging at the point of systemic endothelial dysfunction, hypertension, and proteinuria ***(Iasmina et al., 2014).***

Adrenomedullin (AM) is a potent vasodilator peptide, but known to exert a variety of effects within the cardiovascular system. AM expression is widely distributed throughout the cardiovascular system and has been identified in the heart,

lungs, blood vessels and kidneys. In addition, the co-localization of AM and its receptor components suggest AM acts as an autocrine and/or paracrine factor to play a key role in the regulation of cardiovascular function ***(Nishikimi et al., 2013).***

The possible role of vasoactive peptide Adrenomedullin (AM) is considered in the etiology of PE, where AM is indicated to be a protective factor decreasing blood pressure. Higher AM plasma concentration in women with PE suggests possible correlation between AM level and pathological changes in cardiovascular system during pregnancy ***(Boć-Zalewska et al., 2011).*** It causes hypotension when given peripherally. This peptide essentially dilates the blood vessels improving blood flow in the visceral organs ***(Takahashi et al., 2011)***.

# AIM OF THE WORK

The aim of the present study is to assess serum Adrenomedullin (AM) in a group of pregnant females with preeclampsia (PE) to evaluate its clinical utility in diagnosis and assessment of severity of the disease.

# I-PREECLAMPSIA

## A) Definition:

Preeclampsia (PE) is defined as Maternal blood pressure ≥140/90 on two separate readings at least 4 h apart after 20 weeks of gestation, in a woman with a previously normal blood pressure, or maternal blood pressure ≥160/110, and one of the following:

1) Proteinuria: based on one of the following:
   - i- Greater than or equal to 300 mg per 24-h urine collection (or this amount extrapolated from a timed collection).
   - ii- Protein/creatinine ratio ≥0.3.
   - iii- Dipstick reading of 1 + (used only if other quantitative methods are not available).
2) Thrombocytopenia: platelet count <100 000/µL;
3) Renal insufficiency: serum creatinine concentrations >1.1 mg/dL or a doubling of the serum creatinine.
4) Impaired liver function: elevated blood concentrations of liver transaminases to twice the normal concentrations.
5) Pulmonary oedema.
6) Cerebral or visual symptoms.

***(ACOG, 2013)***

## B) Epidemiology:

PE is around 3–5% of pregnancies in developed countries and up to 7.5% of all pregnancies around the globe ***(Abalos et al., 2013).*** In developing countries, PE is responsible for 12-18 % of pregnancy-associated maternal demise. It affects 4.4% of all deliveries because of illiteracy, lack of health awareness and education, poverty, and false beliefs that avert women from seeking medical care during pregnancy ***(Sablah, 2011)***

## D- Classification of Preeclampsia:

There are many subtypes of PE. Various classifications are used:

### 1-Severity (Mild or Severe Preeclampsia):

Mild PE, which may show no symptoms as many cases are discovered through routine prenatal screening. However, physical examination show elevated blood pressure with two readings of systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, separated by 4 hour period, there is no sign or symptoms of fetal or maternal complication ***(Mann et al., 2011).***

While, severe PE is commonly diagnosed by the presence of one or more of the signs and symptoms listed in (Table-1) ***(Ciantar and Walker, 2011)***.