THROMBOMODULIN LEVEL IN PREGNANCY-INDUCED HYPERTENSION

A Thesis Submitted for Partial Fulfilment of
MASTER DEGREE IN OBSTETRICS & GYNAECOLOGY

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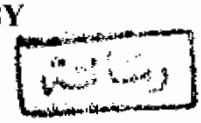

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1995

ACKNOWLEDGMENTS

I wish to express my gratitude to

Professor Dr. ALAA EL DIN MOHAMED KAMAL EL ETRIBY, Professor of Obstetrics & Gynaecology, Ain Shams University, for his overwhelming kindness and continuous advice and support.

I am also deeply indebted to

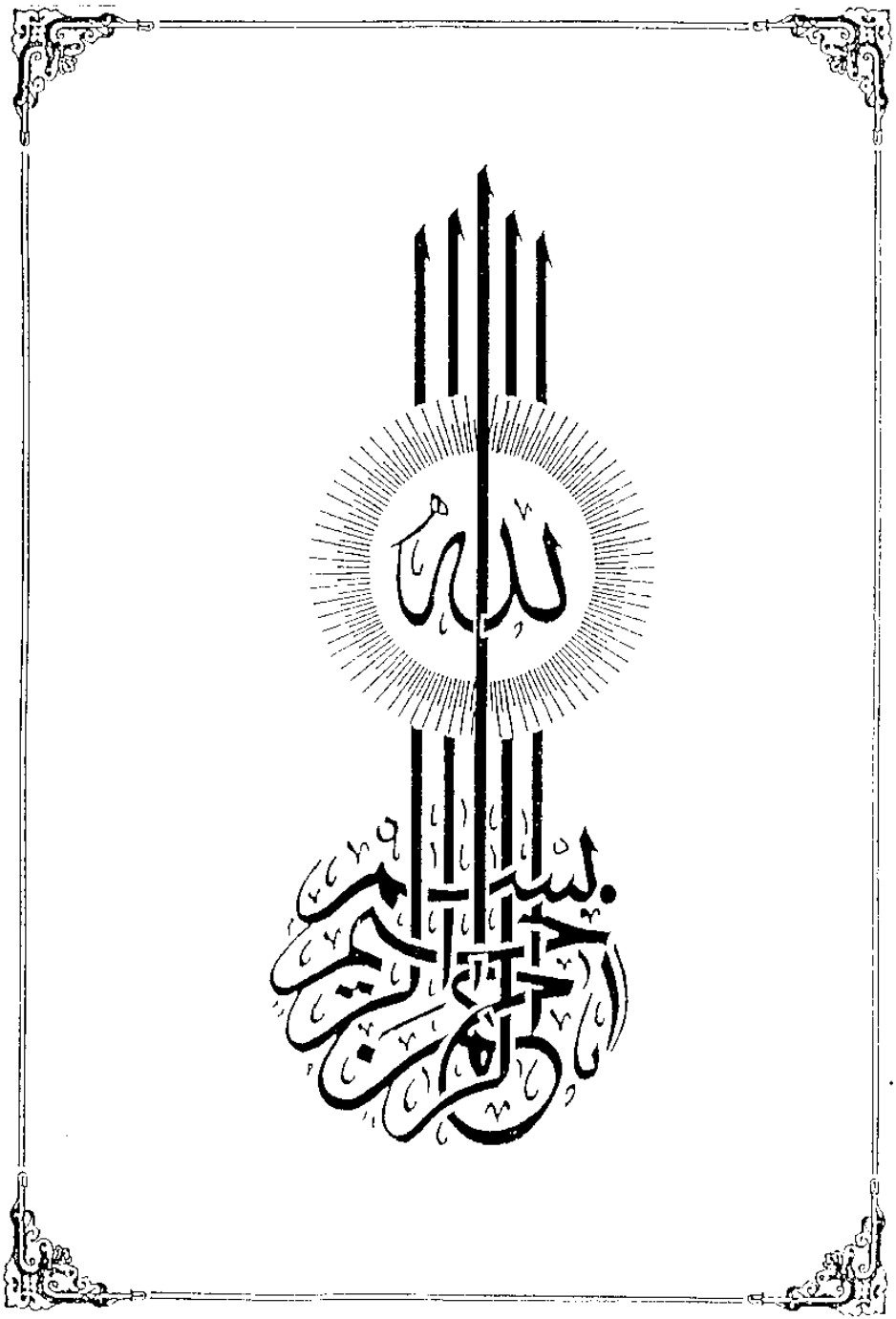
Dr. MOHAMED ASHRAF MOHAMED FAROUK KORTAM, Lecturer of Obstetrics & Gynaecology, Ain Shams University, for his continuous guidance, support and encouragement, during the preparation of this work.

Also, a special appreciation to

Dr. MONA AHMED WAHBA, Lecturer of Clinical Pathology, Ain Shams University, who was always supportive and constructive with all her remarks and advices.

Last, but by no means the least, I would like to thank all the patients, who agreed to participate in this research with their complete understanding and cooperation all through the time of this thesis.

Rami Antoun Wakim
1995



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INTRODUCTION

INTRODUCTION

Preeclampsia is recently considered a part of pregnancy-induced hypertension (PIH). It is a condition peculiar to primate pregnancy, and is rarely manifested before 24-28 weeks gestation. It is characterized by the classic triad of hypertension, oedema and proteinuria. The presence of any two of the triad is accepted as sufficient to make the diagnosis ***(Pernoll et al., 1994).***

Preeclampsia is a disorder of unknown cause and pathogenesis. It has been recently suggested that endothelial cell injury may be implicated in the development of preeclampsia ***(Robert et al., 1989).***

Protein C is activated by thrombin. This activation proceeds very slowly unless it takes place in the presence of thrombomodulin, an endothelial cell surface protein which binds thrombin and markedly enhances the ability of thrombin to activate protein C ***(Owen et al., 1981).***

Thrombin bound to thrombomodulin rapidly activates protein C. Activated protein C inhibits coagulation by inactivation of coagulation factors Va, VIIIa ***(Stern et al., 1986).*** On the other hand, the thrombomodulin-bound thrombin will no longer

activate factor V, bind platelets, or clot fibrinogen. Thus, when thrombin binds to thrombomodulin, it is transformed from a procoagulant into an enzyme which generates activated protein C, a potent anticoagulant ***(Esmon CT et al., 1982; Esmon NL et al., 1983).***

A soluble thrombomodulin antigen has been discovered in human blood and urine after the damage of endothelial cell ***(Ishii et al., 1985).***

Alterations in the levels of thrombomodulin on the endothelial cell surface have the potential to affect the protein C system.

Various inflammatory mediators affect endothelial cell function, as IL-1 which induces the synthesis and expression of tissue factor activity on the endothelial cell surface ***(Moore et al., 1987).***

AIM OF THE WORK:

Assessment of thrombomodulin and its reliability as a marker in cases of PIH.

CHAPTER 1 - 3
REVIEW OF LITERATURE

CHAPTER 1

PREGNANCY -INDUCED HYPERTENSION

Irvin Loudon, (1991) stated that if the cause of a disease is unknown, renaming it thus reflects new theories and produces a comforting illusion of progress. Toxaemia is a prime example .

Since the 18^{th} century, it has appeared under such headings as puerperal convulsions, puerperal nephritis and albuminuria, eclampsia, toxaemia and preeclamptic toxaemia and recently as pregnancy - induced hypertension or hypertensive disease with pregnancy.

The term pregnancy - induced hypertension (PIH) will be used in this study.

Pregnancy can induce hypertension in normotensive women or aggrevate already existing hypertension . Generalised edema proteinuria or both may also accompany pregnancy - induced or aggrevated hypertension. Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with haemorrhage and infection, that results in a large number of maternal deaths. ***(Cunnigham et al, 1993)***

Compared with normotensive gravidas, patients with elevated blood pressure have significantly greater maternal and fetal mortality and morbidity. ***(Ferrazzani et al, 1990)***

Definitions:

Pregnancy - induced hypertension is defined as hypertension that develops as a consequence of pregnancy and regresses post-partum.

This definition was proposed by the American College of Obstetricians and Gynecologists (ACOG) in 1986 and was done to separate hypertension that is in some way induced by pregnancy from hypertension that merely coexists with it.

Additionally, it had also proposed the following definitions:

- Pregnancy aggrevated hypertension as underlying hypertension worsened by pregnancy.
- Coincidental hypertension as chronic underlying hypertension that antecedes pregnancy or persists post-partum.
- Transient hypertension as elevated blood pressure during pregnancy or in the first 24 hours post-partum without other signs of preeclampsia or coincidental hypertension.
- Preeclampsia as development of hypertension with proteinuria or edema or both, induced by pregnancy after the 20th week of gestation.
- Superimposed preeclampsia as preeclampsia that develops in a woman with chronic hypertensive vascular or renal disease. ***(Cumingham et al, 1993)***

Classifications :

Several classifications were designed for hypertensive disorders in pregnancy accompanied by proteinuria or edema.

An old one was proposed by ***Patterson, (1975):***

EPH - Gestosis.

Nomenclature, Definitions and Classifications of EPH-Gestosis :

Nomenclature EPH-GESTOSIS

Pregnancy = Gestatio

Complicated ... = ... Osis

..... by

E = Edema

P = Proteinuria

H = Hypertension

EPH-Gestosis

Definitions

E = Edema	Excessive (inadequate) increase of body-weight during pregnancy, usually due to fluid retention, i.e. more than 500 g/week 2000 g/month 13 kg/entire pregnancy Demonstrable pretibial edema are of gestosis origine, if they are still present after a night's bedrest.
P = Proteinuria	Protein in the 24 hours-urine specimen, more than 0.5‰ Esbach (or similar quantitative test, like paper stick) is pathological.
H = Hypertension	Last normal reading135/85mmHg. First pathological reading 140/90 mm Hg. In primary hypertension rise of 30 mm Hg or more systolic and/or rise of 15 mm Hg or more diastolic.