THE ROLE OF INCREASED THROMBOXANE LEVEL IN BLOOD OF DIABETIC PREGNANCIES AS A POSSIBLE CONTRIBUTOR TO PREECLAMPSIA

THESIS

Submitted for Partial Fulfilment of
Master Degree in
OBSTETRICS & GYNECOLOGY

BY

AYMAN MAHMOUD EL-NAQA
M. B B. Ch. (Ain Shams)

SUPERVISED BY

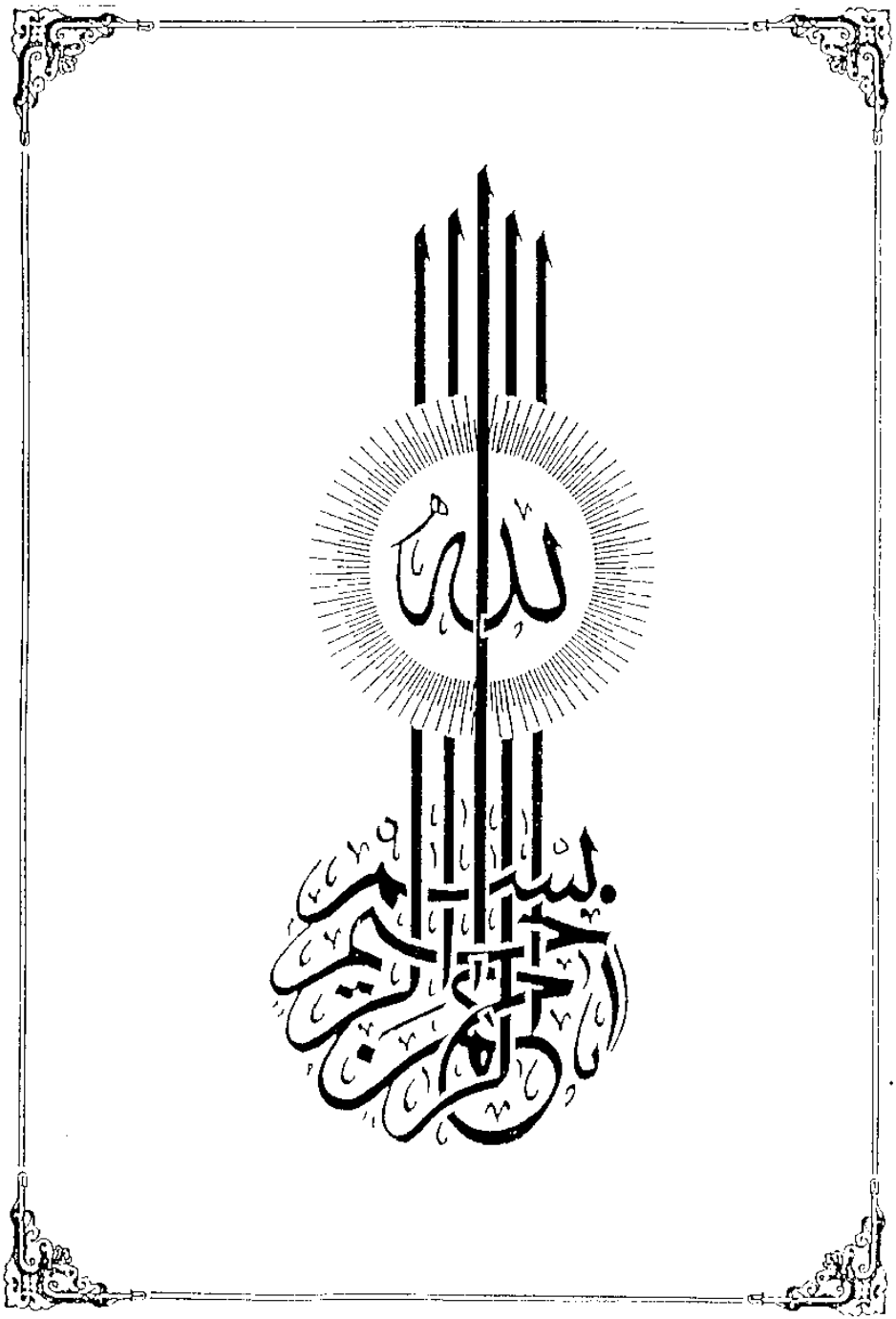
Prof. Dr. HAMDY EL KABARITY
Professor of Obstetrics & Gynecology.
Ain Shams University

Prof. Dr. MOUSTAFA EL-RASAD
Professor of Biochemistry
Ain Shams University

Dr. SHREIF A. AKL
Lecturer of Obstetrics & Gynecology
Ain Shams University

Faculty of Medicine
AIN SHAMS UNIVERSITY
(1994)


بسم الله الرحمن الرحيم



ACKNOWLEDGMENT

Thanks God who allowed and helped me to accomplish this work.

I wish to express my deepest gratitude and appreciation to ***Prof. Dr. HAMDY EL-KABARITY,*** *Professor of Obstetrics and Gynecology, Ain Shams University, for his constant supervision, valuable suggestions, encouragement and his fatherly attitude was a great help to complete this work.*

My special thanks and appreciation for ***Prof. Dr. MOUSTAFA EL-RASAD,*** *Professor of Biochemistry, Ain Shams University, for his kind supervision, encouragement and moral support.*

My sincere thanks are to ***Dr. SHREIF AKL,*** *Lecturer of Obstetrics and Gynecology, Ain Shams University, for his kind supervision, patient guidance, valuable advices, generous help and revising all the details of this work.*

I also wish to express my gratitude to ***Dr. NASHWA EL-KHAZRAGGY*** *and her colleagues in the Tumour Marker Unit, Ain Shams University, for their great help and effort in the laboratory work of this study.*

Last but not least, I would like to thank my patients, my colleagues and every one participated in some way or another in making this work feasible.

CONTENTS

	Page
INTRODUCTION	1
AIM OF THE WORK	
REVIEW OF LITERATURE	
• Diabetes Mellitus in Pregnancy	4
• Epidemiology and Etiology of Preeclampsia	28
• Prostaglandins	44
MATERIAL AND METHODS	69
RESULTS	76
DISCUSSION	107
RECOMMENDATION	111
SUMMARY	112
APPENDIX	114
REFERENCES	120
ARABIC SUMMARY	---

INTRODUCTION

INTRODUCTION

The main objectives of an obstetrician managing cases of pregnancy induced hypertension are prevention and early detection to improve fetal and maternal out come and this becomes of great importance in diabetic patients.

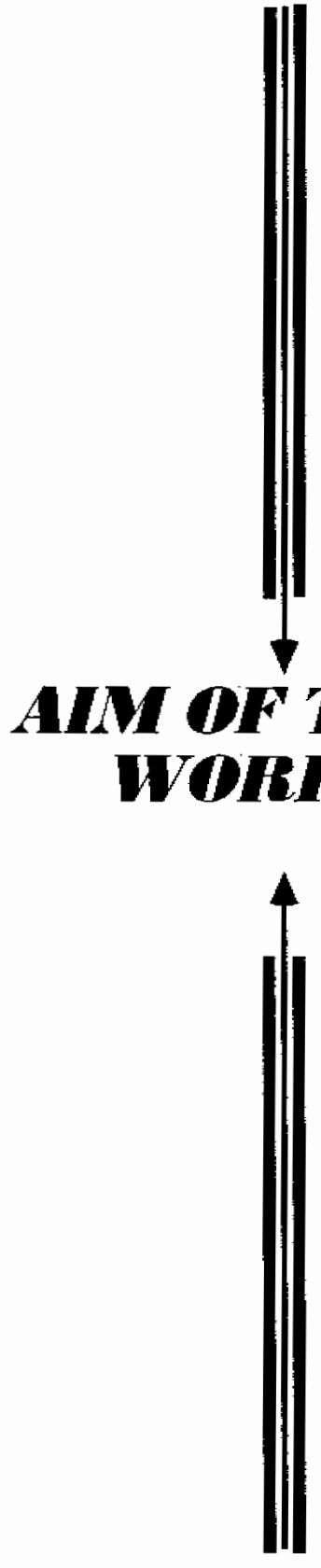
Preeclampsia affects approximately up to 7% of all pregnancies this is responsible for 70% of all hypertension occurring in pregnancy *(Barton et al., 1991)*.

Pregnant diabetic patients have an increased incidence of preeclampsia. Recently, preeclampsia was found in 9.9% of diabetic pregnancies, compared with 4.35% in controls. The incidence is more in the type I diabetic pregnancies and the incidence increased with the severity of diabetes *(Garner et al., 1990)*.

Fitzgerald & co-workers have demonstrated markedly higher urinary excretion of thromboxane A_2 (TX A_2) metabolites in eight patients with pregnancy induced hypertension in comparison with six normotensive pregnant women. They

suggested that TX A_2 biosynthesis is increased and may have a role in pathogenesis of pregnancy induced hypertension. *(Fitzgerald et al., 1990).*

The increased capacity of platelets of diabetics to produce TX A_2 together with the "physiologic' platelet activation of pregnancy could explain the high levels of TX A_2 metabolites in the pregnant diabetic women. *(F. Andre Van Assche et al., 1993).*


AIM OF THE
WORK

AIM OF THE WORK

Because pregnant women with diabetes have an increased incidence of preeclampsia. The aim of this study is to support the role of thromboxane in the pathogenesis of preeclampsia, by testing the serum levels of TX A_2 metabolites in diabetic pregnancies without evidence of preeclampsia at the time of testing.

REVIEW OF LITERATURE

DIABETES MELLITUS IN PREGNANCY

DIABETES MELLITUS

Definition :

Diabetes mellitus is a common condition world wide and the term encompasses a heterogenous group of clinical and biochemical disorders of varying etiology, severity and treatment, characterized by the common metabolic feature of hyperglycemia. An abnormally raised blood glucose level results from an absolute or relative deficiency of the hormone insulin, or resistance to the metabolic action of insulin, and the clinical manifestations depend on the underlying metabolic derangements *(Pearson et al., 1991).*

The metabolic disturbances affect the carbohydrate, protein, fat, water and electrolytes and lead eventually, in many cases, to cellular damage, specially to vascular endothelial cells, in the eye, kidney and nervous system.*(Brudnell and Doddridge, 1989).*

Prevalence of Diabetes Mellitus in Pregnancy :

Being one of the commonest medical complication of pregnancy, diabetes mellitus attracted the interest of obstetricians and public. The cause for remarkable increase in

recent years are not known, but environmental factors as well as genetic predisposition are implicated.

As agreed by most, pregnancy is complicated by diabetes mellitus in abut 3% of all cases *(Mestaman et al., 1980).*

The principle for incriminating environmental factors is provided mainly by the observations that for many young patients with insulin dependant diabetes, there is no family history of diabetes. Moreover, the concordance rate for diabetes in monozygotic twins rather than being nearly 100% if diabetes was solely genetic in origin, is less than 50% *(Foster, 1991).*

Probably there is an interaction between environmental factors, specially viral and genetic predisposition. An association has been found between the human leucocytic antigen (HLA) system and some but not all forms of diabetes *(Foster, 1991).*

Classification :

Many classifications have been proposed which are abit confusing; but in general, women whose pregnancies are complicated by diabetes can be separated into those who are

known to have diabetes before pregnancy and those with gestational diabetes.

These classifications include :

1) W. H. O. classification.
2) White classification.
3) National Diabetes Data Group classification.

W. H. O. Classification

A) Potential Diabetes :

These patients have normal glucose tolerance test (G.T.T) but still have increased risk to develop diabetes due to risk factors.

a) One parent or both are diabetics.
b) An identical twin, the other being diabetic.
c) Giving birth to heavy baby 4.5 kg or more.
d) Giving birth to diabetic sibling.

B) Latent diabetes :

Normal G.T.T. currently, but has been either a diabetic G.T.T. or abnormal blood glucose response to provocative tests.

C) Chemical Diabetes :