

THE STUDY OF SERUM FERRITIN IN PATIENTS WITH GESTATIONAL DIABETES

Thesis

*Submitted for Partial Fulfillment of
Master Degree in Obstetrics and Gynaecology*

BY

Laila Aly Farid Mohamed Aly
M.B.B.Ch., Ain Shams University
Resident of OB/GYN,
Ain Shams University Maternity Hospital

Supervised by

Dr. Helmy Metawe El-Sayed
Assistant Professor of Obstetrics & Gynecology
Faculty of Medicine - Ain Shams University

Dr. Ahmed Mohamed Ibrahim
Lecturer of Obstetrics & Gynecology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2007

دراسة نسبة مادة الفريتين بالدم في الحوامل المريضات بداء البول السكري المصاحب للحمل

رسالة توطئة للحصول على درجة الماجستير في أمراض النساء والتوليد
مقدمة من

الطبيبة/ ليلي على فريد
بكالوريوس الطب والجراحة - جامعة عين شمس
طبيب مقيم أمراض نساء وولادة
مستشفى أمراض النساء والولادة - طب عين شمس

تحت إشراف

الدكتور / حلمي مطاوع السيد

أستاذ مساعد أمراض النساء والتوليد
كلية الطب - جامعة عين شمس

الدكتور / أحمد محمد إبراهيم

مدرس أمراض النساء والتوليد
كلية الطب - جامعة عين شمس

كلية الطب
جامعة عين شمس
٢٠٠٧

II

ولقد خلقنا الانسان من سلاله من طين {12} ثم
جعلناه نطفه في قرار
مكين {13} ثم خلقنا النطفة علقه فخلقنا العلقه
مضغه فخلقنا المضغه عظاماً فكسونا العظام
لحماً ثم أنشأناه خلقاً آخر فتبارك الله أحسن
الخالقين {14}

ω

سورة المؤمنون الآيات 12-13-14

Acknowledgement

First of all,

Thanks to GOD who allowed and helped me to accomplished this work.

I owe special gratefulness and much regards to **Dr. Helmy Metawe El-Sayed**, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, to whom I owe more than words can express. His limitless help, valuable advise and kind encouragement.

I would like to display my very indebtedness to **Dr. Ahmed Mohamed Ibrahim**, Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his constructive supervision and his help in constructing the work. I received a great deal of help from him, that words cannot express.

Laila Aly Farid Mohamed Aly

Contents

<i>Title</i>	<i>Page</i>
• Introduction.....	1
• Aim of the Work.....	4
• Review of Literature.....	
- Gestational Diabetes Mellitus.....	5
- Iron Metabolism.....	38
• Patients and Methods.....	81
• Results.....	87
• Discussion.....	103
• Summary.....	108
• Conclusion.....	111
• References.....	112
• Arabic Summary	

List of Tables

Table No.	Title	Page No.
1	Fourth international workshop conference on gestational diabetes: Recommended screening strategy based on risk assessment of detecting gestational diabetes.....	10
2	American College of Obstetricians and Gynecologists 2001 criteria for Diagnosis of Gestational Diabetes using 100-gm oral glucose tolerance test.....	11
3	Post-partum evaluation for glucose intolerance in women with gestation diabetes.....	29
4	Iron balance in pregnancy.....	49
5	Comparison between demographic data (age, parity and GA) in control cases and diabetic patients.....	87
6	Comparison between demographic data (age, parity and GA) in control cases, controlled diabetic patients and uncontrolled diabetic patients.....	88
7	Comparison between liver function tests in controls and diabetic cases.....	90
8	Comparison between liver function tests in control cases and diabetic controlled patients and diabetic uncontrolled patients.....	91
9	Comparison between hemoglobin level in control cases and diabetic cases.....	92
10	Comparison between hemoglobin level in control cases, diabetic controlled cases & diabetic uncontrolled cases.....	93
11	Post HOC Tests to determine the significant difference between control cases, diabetic controlled cases & diabetic uncontrolled cases as regards hemoglobin level, serum iron, total iron binding capacity and serum ferritin.....	94
12	Comparison between iron profile (serum iron, TIBC and serum ferritin) in control cases and diabetic patients.....	99
13	Comparison between iron profile (serum iron, TIBC and serum ferritin) in control cases, controlled diabetic patients and uncontrolled diabetic patients.....	101
14	Correlation between serum iron, serum ferritin and blood glucose level.....	102

List of Figures

Fig. No.	Title	Page No.
1	Part of a 24-subunit model of a ferritin molecule showing iron-core crystalline adhering in random orientations to the inner protein surface.....	56
2	Diffuse X-ray pattern of the ferritin micelle in cubic crystals.....	57
3	Model of ferritin showing probable subunit arrangement (24 subunits at apices of a snub cube). The iron core (shown dark) can be seen through the inner subunit spaces...	58
4	Schematic representation of iron interactions with insulin resistance and oxidative stress.....	68
5	Mean values of haemoglobin among cases and controls.....	92
6	Mean values of haemoglobin among diabetics controlled, uncontrolled and controls.....	96
7	Mean values of serum iron among diabetics controlled, uncontrolled and controls.....	96
8	Mean values of TIBC among diabetics controlled, uncontrolled and controls.....	97
9	Mean values of serum ferritin among diabetics controlled, uncontrolled and controls.....	97
10	Mean values of serum iron among cases and controls.....	99
11	Mean values of TIBC among cases and controls.....	99
12	Mean values of serum ferritin among cases and controls.....	99

Introduction

INTRODUCTION

The pathogenesis of gestational diabetes is not fully understood as multiple factors including genetic factors, environmental events, obesity, insulin resistance and islet cell abnormality, appear to be involved. One of these factors may be an excessive absorption and storage of dietary iron. Emerging scientific evidence has disclosed unsuspected influences between iron metabolism and gestational diabetes (*Bertelsen et al., 2001*).

Recently, many studies aimed at studying the relation between iron metabolism, serum ferritin and the prevalence, diagnosis, control and development of complications in pregnant diabetic patients. The model upon which this concept is based is idiopathic haemochromatosis in which diabetes is an early complication in about 60% of the affected persons (*Dymock et al., 1972*).

It has been postulated that iron accumulation in hepatocytes may interfere with the liver insulin-extracting capacity. Supporting evidence comes from studies in non cirrhotic hemochromatotic patients. In these patients, insulin resistance and hyperinsulinemia appeared before pancreatic iron overload with selective B cell loss occurred (*Dymock et al., 1972*).

A second suggestion is that iron deposition may cause insulin resistance by interfering with the ability of insulin to suppress hepatic glucose production (*Fernandez-Real et al., 1998*). This theory may explain the relationship between

insulin resistance and high ferritin level (***Fernandez-Real et al., 1998***).

Also it is believed that increased blood glucose in DM stimulates non enzymatic glycosylation of several proteins including Hb. Studies with purified Hb from normal individual and diabetic patients revealed that concentration of free iron was significantly higher in latter cases with increased progressively with extent of the disease.

In vitro glycosylation of Hb also lead to increase in release of iron from protein. This increase in free iron, acting as a fenton reagent might produce free radicals which in turn might be causing oxidative stress in diabetes (***Fujimoto et al., 1995***).

As well, these highly reactive free radicals peroxidize lipids which change membrane proteins and result in tissue damage. Increased oxidation of free fatty acids was also found to diminish glucose utilization in muscle tissue and to increase gluconeogenesis in the liver leading to increased insulin resistance (***Oberley, 1988***).

Indeed, serum level of lipid peroxidation substances was high in patients with diabetes and diabetic microangiopathy (***Loebstein et al., 1998***).

Unfortunately, studies on this subject have yielded conflicting results. Some results has shown a positive correlation between plasma ferritin and poor metabolic control, others have not (***Fernandez-Real et al., 1998; Oba et al., 1997***). Other studies concluded that hyperferritinemia is a

feature of newly diagnosed diabetes (*Dinneen et al., 1992*) but not of established disease with poor control similar compelling results were also found in studies with type I DM patients (*Gallou et al., 1994*).

The finding of a definite relationship between iron metabolism and diabetes may help in defining the value of iron supplementation during pregnancy and improving that while iron supplementation may improve pregnancy outcome when the mother is iron deficient, it is also possible that prophylactic supplementation may increase risk when the mother doesn't have iron deficiency. It will also help in evaluating the capability of usage of deferoxamine in treating diabetic patents with a mild-moderate increase of serum ferritin (*Redmon et al., 1993*).

In this study, we are trying to find out this relationship and to solve the confliction.

Aim of the Work

AIM OF THE WORK

In this study, the plan is:

- 1- To determine whether non-anaemic women with gestational diabetes mellitus (GDM) diagnosed in third trimester pregnancy have evidence of increased iron stores compared with matched non-diabetic controls.
- 2- To investigate relationship between diabetes control and serum ferritin.

Review of Literature

Chapter 1

GESTATIONAL DIABETES MELLITUS

Gestational diabetes mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy. It does not exclude the possibility that the glucose intolerance may have antedated pregnancy (*Gobbe, 1986*).

Glucose tolerance deteriorates in all pregnant women but only in 2-38 of all pregnancies is the deterioration sufficiently large to fulfill the diagnostic criteria for gestational diabetes. There is no doubt that gestational diabetes must be considered to be a disease entity that presents significant perinatal risks and carries an enhanced risk for the later development of manifest diabetes in the mother. There is growing evidence, however that the perinatal risks can be reduced or even abolished by a systematic approach to the identification and management of this disorder (*Kühl, 1991*).

The recognition that diabetes results in a disturbance of the environment of the foetus that may seriously interfere with organogenesis and development had led to an acknowledgment that normoglycaemia is an important objective in diabetic control. Until this can be achieved before conception and throughout the early part of pregnancy, there seems little likelihood that it will be possible to reduce the increased incidence of congenital malformation that threatens the pregnancy of every woman with established diabetes: