# Relation between Homocysteinemia and Diabetic Retinopathy in Patients with Type 2 Diabetes

Thesis Submitted for Partial Fulfillment of Master Degree in Endocrinology
By

Tamer Fawzy Zaky EL Gohary

**Under the Supervision of** 

Doctor: Salah Shelbaya

Professor of Internal Medicine and Endocrinology

Faculty of Medicine Ain Shams University

**Doctor: Hanan Amer** 

Assistant Professor of Internal Medicine and Endocrinology
Faculty of Medicine

Ain Shams University

**Doctor: Abeer Ahmed** 

Lecturer of Internal Medicine and Endocrinology
Faculty of Medicine
Ain Shams University

2006

# Relation between Homocysteinaemia and Diabetic Retinopathy in Patients with Type 2 Diabetes

Thesis Submitted for Partial Fulfillment of Master Degree in Endocrinology
By

Tamer Fawzy Zaky EL Gohary

**Under the Supervision of** 

Doctor: Salah Shelbaya

Professor of Internal Medicine and Endocrinology

Faculty of Medicine Ain Shams University

Doctor: Hanan Amer

Assistant Professor of Internal Medicine and Endocrinology
Faculty of Medicine

Ain Shams University

**Doctor: Abeer Ahmed** 

Lecturer of Internal Medicine and Endocrinology
Faculty of Medicine
Ain Shams University

2005

#### **Introduction:**

Homocysteine, a substance the body normally turns into amino acids by vitamin B12 and folic acid, came into the limelight few years ago. (John Walsh et al., 2003).

An association between severely increased serum Homocysteine and the early atherosclerotic disease has long been recognized. (Giles et al., 2000)

Recent researches discovered that Homocysteine can directly damage blood vessels and is strongly associated with heart attacks, strokes, and peripheral vascular disease. Homocysteine attaches to LDL and modifies its structures much like oxidation and glycosylation do. This modification of LDL by Homocysteine seems to accelerate heart disease. (John Walsh et al., 2003).

As macrovascular disease is a common complication of diabetes, studies have been directed to the role of Homocysteine and incidence of cardiovascular disease in diabetes. (Looker et al., 2003)

In addition, associations have been suggested between Homocysteine in diabetic subjects and the prevalence of micro vascular disease, such as retinopathy. (Vaccaro, 2000)

There is evidence that Homocysteine can cause apoptosis in retinal ganglion cells in mice. In vitro work has suggested that this damage could be potentate in the presence of hyperglycemia. (Vaccaro, 2000)

## **Aim of the work:**

Is to assess the role of plasma homocysteine as a risk factor for retinopathy in type 2 diabetes.

## **Subject and Methods:**

This study will be conducted on 4 groups:

- **Group I:** 15 type 2 diabetic patients without retinopathy (noDR)
- **Group II:** 15 type 2 diabetic patients with non proliferative retinopathy (NPDR)
- **Group III:** 15 type 2 diabetic patients with proliferative retinopathy (PDR)

Group IV: 15 control subject

## All were subjected to:

### -Full history taken

With special stress on:

- Age to be above 40 yrs.
- Sex.
- Duration of diabetes.
- History of hypertension and antihypertensive medications.

## -Full clinical examination

With special stress on:

- blood pressure
- B M I
- Estimation of Retinopathy by fundus examination.

## -The following investigations were done:

- Glycated hemoglobin.
- Serum creatinine.
- Vitamin B12.
- Plasma Homocysteine.

#### **References:**

- Giles WH, Greenlund KJ, Ford ES et al., (2000): Association between total Homocysteine and the likelihood for history of acute myocardial infarction by race and ethnicity: results from the third National Health and nutrition Examination survey Am Heart j 139:446-453.
- Jager A, kostense PJ, Nijpels G et al., (2001): serum Homocysteine level is associated with the development of microalbuminuria: The Hoorn study. Arterioscler Thromb Vasc biol 21:74-81
- John Walsh, P.A. and Ruth Roberts, M.A. (2003): Homocysteine as risk factor for nephropathy and retinopathy in type 2 diabetes, Diabetes Services, Inc.
- looker.H.C,Fagot.A,Gunter.et al ., (2003): Homocysteine as risk factor of nephropathy and retinopathy in type 2 diabetes, Diabetologia (2003) 46:766-772.
- Vaccaro O, Perna AF, Maccini FP et al., (2000): Plasma Homocysteine and microvascular complication in type1 diabetes. Nutr Metab Carrdovasc Dis 10:297-304.

## العلاقة بين الهوموسيستين وإعتلال الشبكية

## الناتج عن مرض السكر في المرضى من النوع الثاني

## تامر فوزى زكى الجوهرى

## الأستاذ الدكتور: صلاح شلبايه

أسناذ الباطنه والغدد الصماء كليت الطب - جامعتر عين شمس

## دكتورة: حنان عامر

أسناذ مساعد الباطند والغدد الصماء كليترالطب – جامعترعين شمس دكنورة: عبير أحمد مدرس الباطند والغدد الصماء كليترالطب – جامعترعين شمس 2005

12

0

0

15: .(

15: 15: 15: 40 ) • ( 12

First, thanks to *God* for blessing this work and for his care and generosity throughout my life.

I am greatly honored to express my deep thanks and profound gratitude to professor DR. Salah Shelbaya, Professor of Internal Medicine and Endocrinology, Ain Shams University, to whom I am deeply indebted for encouraging me to develop this work, and for the valuable supervision and continuous help, he has given me since I started this work.

I would like to state great appreciation to Dr. Hanan Amer, Assistant Professor of Internal Medicine and Endocrinology, Ain Shams University, for her valuable instructions, inspiring guidance and support throughout this work.

I sincerely appreciate all the encouragement and support given by **Dr Abeer Ahmed**, Lecturer of Internal Medicine and Endocrinology, Ain Shams University.

Lastly, I would like to express my deepest appreciation to all professors in the internal medicine and endocrinology department, Ain Shams University, for all their precious support during my work and training.

#### **Contents**

•	Introduction and aim of the work	1	
•	Review of Literature		
	Chapter I: Diabetic Retinopathy	3	
	Chapter II: Homocysteine	36	
	Chapter III: Hyperhomocysteinemia & Diabetic Retinopath		
•	Subject & Method	87	
•	Results	97	
•	Discussion	122	
•	Summary and Conclusion	133	
•	Recommendations	136	
•	References	137	
•	Arabic summary		

### **Review of literature:**

Tables #	Subjects	Page
	International Clinical Diabetic	15
1	Retinopathy Disease Severity Scale.	
	Management Recommendations for	
2	Patients with Diabetic retinopathy	31
3	<b>American Diabetes Association</b>	
	recommendations for glycemic control	33

#### **Results:**

Tables #	Subjects	Page
1	Descriptive data regarding clinical parameters in all studied groups	106
2	Comparison between noDR group & control group	
3	Comparison between NPDR group & control group	
4	Comparison between PDR group & control group	109
5	Comparison between noDR group & NPDR group	110
6	Comparison between no DR group & PDR group	111
7	Comparison between NPDR group & PDR group	112
8	8 Comparison between all diabetics & control group	
9	Comparison between diabetics with &without retinopathy	114
10	Correlation between plasma homocysteine and all studied parameters in all diabetic patients	119
11	Correlation between plasma homocysteine and all studied parameters among all groups.	120
12	Mean homocysteine level and Prevalence of hyperhomocysteinemia among all studied groups	121

## List of Figures

Figures #	Subjects	Page
1	Metabolic pathways implicated in the development of diabetic microvascular complications	11
2	Publications on homocysteine	37
3	Chemical Structure of Homocysteine.	38
4	Metabolism of Homocysteine.	42
5	Schematic representation of the metabolism of Hcy, and Hcy thiolactone.	43
6	Distribution of various forms of homocysteine in plasma.	47
7	Effect of age and gender on Hcy concentrations.	50
8	Dose-response relationship between vitamin concentrations and plasma tHcy	65
9	Determinants of plasma homocysteine	73
10 Hyperhomocysteinemia and diabetic complications		81

## Results:

Figures #	Subjects	Page
1	Comparison between all studied groups regarding mean levels of homocysteine.	115
2	Comparison between all studied groups regarding vitamin B12.	116
3	Comparison between studied groups regarding mean duration of diabetes.	117
4	Comparison between males and females among all studied groups regarding mean levels of homocysteine	118
5	Correlation analysis between plasma homocysteine and HbA1c among all studied groups.	122
6	Correlation analysis between Vitamin B12 and HbA1c among all studied groups.	122
7	Correlation analysis between plasma homocysteine and Vitamin B12 among all studied groups.	123