

**Study of Soluble E-selectin in patients
With IDDM and NIDDM;
relation to metabolic control**

Thesis

**Submitted for the Partial Fulfillment
of M.Sc Degree (Internal Medicine)**

By

Lamiaa Ahmed Hachishe

M.B., B.Ch.

Supervisors

Prof. Dr./ Hussein El Damasy

Professor of Internal Medicine & Endocrinology
Faculty of Medicine - Ain Shams University

Prof. Dr./ Salah Shelbaya

Professor of Internal Medicine & Endocrinology
Faculty of Medicine - Ain Shams University

Dr. Nihad Shoeib

Lecturer of Internal Medicine & Endocrinology
Faculty of Medicine - Ain Shams University

**Faculty of Medicine
Ain Shams University
1998**





بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿فَوْقَ كُلِّ ذِي عِلْمٍ﴾

صَدَقَ اللَّهُ الْعَظِيمُ

Contents

I.	Introduction	1
II.	Aim of the Work	2
III.	Review of Literature	3
	Chapter I: Non-Insulin-Dependent Diabetes Mellitus	
	• Genetics of NIDDM	3
	• Pathogenesis of NIDDM	5
	I. Impaired Insulin Secretion	6
	II. Insulin Resistance in NIDDM	11
	Chapter II: Insulin-Dependent Diabetes Mellitus	
	• Definition	23
	• Epidemiology	24
	• Pathogenesis (Etiologic classification of IDDM)	25
	• The Role of Cell Adhesion Molecules in the development of IDDM	61
	Chapter III: Microvascular Complications of Diabetes Mellitus	
	• Introduction	64
	• Diabetic Retinopathy	66
	- Incidence	66
	- Classification	67
	- Pathogenesis	67
	• Diabetic nephropathy	68
	- Definition	68
	- Classification	69
	- Pathogenesis	69
	• Diabetic Neuropathy	70
	Pathogenesis	70

Chapter IV: Macrovascular Complications of Diabetes Mellitus

- Introduction 72
- Mechanisms of lipid accumulation by macrophages 73
 - A. Receptor Mediated Uptake of lipoproteins 74
 - B. Non-Receptor Mediated Uptake of Lipoproteins 75
- Immune mechanisms of atherosclerosis in diabetes mellitus 80
- The Role of Modified Lipoproteins, Lipoprotein Immune Complexes and Cholesterol Homeostasis in Atherogenesis 81
- Relevance of Modified Lipoproteins, LDL-Immune Complexes, and Macrophage Activation to Atheroma Formation 84
- Role of Cytokines and Growth Factors in Atherogenesis 86
- Plasma Lipid and Lipoprotein Disorders in IDDM and NIDDM 87
 - Quantitative and Qualitative lipoprotein abnormalities in IDDM and NIDDM 92
- Risk Factors of Atherosclerosis 97

Chapter V: Adhesion - Molecules

- Classification of Cell Adhesion Molecules 107
 - The Selectin Family 107
 - The Integrin Family 119
 - The Immunoglobulin Gene superfamily (IGSF) 122

Chapter VI: E-selectin and Diabetes Mellitus

- Introduction 130
- Atherosclerosis and the Adhesion Molecules 130
- E-selectin and Atherosclerotic Cardiovascular disease in diabetes 131

• E-selectin and IDDM and NIDDM relation to metabolic control	132
IV. Subjects and Methods	136
V. Statistical Analysis	151
VI. Results	176
VII. Discussion	181
VIII. Summary	193
IX. Conclusion	195
X. Recommendation	195
XI. References	196
XII. Arabic Summary	

List of Abbreviation

- ADCC = Antibody-Dependent Cellular Cytotoxicity.
- A.GEs = Advanced glycation end products.
- AIDS = Acquired Immune Deficiency Syndrome.
- A.Ms = Adhesion molecules.
- Apo = Apolipoprotein.
- AP.S = Autoimmune Polyendocrine Syndrome.
- A.R. = Aldose reductase.
- Arg = Arginine.
- Asp = Aspartate.
- A.S.Ps = Affected sibling pairs.
- BAL = Bronchoalveolar lavage.
- BMI = Body Mass Index.
- cAMs = cell adhesion molecules.
- C'AMC = Cytotoxic Islet Cell Antibodies.
- = Cytotoxic Antibody mediated cellular cytotoxicity.
- CD = Cluster of Differentiation.
- cELAM-1 = Cell endothelial leukocyte adhesion molecule-1.
- CHD = Coronary Heart Disease.
- CMV = Cytomegalovirus.
- CO = Carbon monoxide.
- CSFs = Colony-Stimulating Factors.
- EBV = Epstein-Barr Virus.
- ECs = Endothelial cells.
- EGF = Endothelial growth factor.
- EFAs = Free fatty acids.
- GABA = Gamma amino butyric acid.

- GAD = Glutamic acid decarboxylase.
- GLUT-2 = Glucose transporter -2.
- GM-CSF = Granulocyte macrophage - colony stimulating factor.
- HDL = High density lipoprotein.
- HGP = Hepatic glucose production.
- HIV = Human immune deficiency virus.
- HLA = Human leukocyte antigen.
- H₂O₂ = Hydrogen peroxide.
- IA = Insulin antibodies.
- IAA = Insulin autoantibodies.
- IBD = Identical-by-descent.
- ICA = Islet-cell antibodies.
- ICAM = Intercellular adhesion molecule.
- ICSA = Islet Cell Surface Antibodies.
- IDDM = Insulin-dependent diabetes mellitus.
- IDL = Intermediate density lipoprotein.
- IgG = Immunoglobulin Gamma.
- IGSF = Immunoglobulin Gene Super Family.
- IGT = Impaired Glucose Tolerance.
- IL-1 = Interleukin-1
- INCAM-110 = Inducible cell adhesion molecule - 110.
- INS = Insulin
- IRS-1 gene = Insulin Receptor Substrate-1 gene.
- LAD = Leukocyte adhesion deficiency.
- LDL = Low-density lipoproteins.
- LFA-3 = Leukocyte function associated antigen -3.
- LNs = Lymph nodes.
- Lp(a) = Lipoprotein (a).

