بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـــسـم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد اعدت دون آية تغيرات

يجب أن

تحفظ هذه الأفلام بعيداً عن الغبار

في درجة حرارة من 15 – 20 مئوية ورطوبة نسبية من 20-40 %

To be kept away from dust in dry cool place of
15 – 25c and relative humidity 20-40 %

بعض الوثائق الأصلية تالفة

بالرسالة صفحات

لم ترد بالأصـــل

ROLE OF TNF-α AND ANTICYTOKINES "PENTOXIFYLLINE" IN DIABETIC NEPHROPATHY WITH MICROALBUMINURIA

Thesis

Submitted to the Faculty of Medicine

University of Alexandria

In Partial Fulfillment of the Requirements

For the Degree of

Master of

Internal Medicine

By

Lamya Ahmed El-Ghlied

M.B.B.CH., (Alexandria)

Medical Research Institute

University of Alexandria

2002

تمت مناقشة الرسالة بطريقة علنية بتاريخ ٤/٤/٢٠٠٤ وقررت اللجنة
قبول الرسالة بتقدير ممتاز ١٠٠٪ (مائة في المائة)
أعضاء اللجنة

SUPERVISORS

Professor Dr. Nader M. Mowafy

Professor of Internal Medicine

Medical Research Institute

University of Alexandria

Professor Dr. Yehia M. Ghanem

Professor of Internal Medicine

Faculty of Medicine

University of Alexandria

Dr. Eman Salah El-Din Khalil

Lecturer of Internal Medicine

Medical Research Institute

University of Alexandria

Co-Worker

Prof. Dr. Mona H. Kandil

Professor of Chemical Pathology

Medical Research Institute

University of Alexandria

ACKNOWLEDGEMENT

Thanks to god who gave me the power to carry out this work honestly and faithfully.

I feel a deep sense of gratitude to prof. Dr. Nader M. Mowafy Professor of internal Medicine Medical Research Institute for his continued support and encouragement. From the very first to the very last day of the work.

Prof. Dr. Yehia M. Ghanem Professor of internal Medicine Faculty of medicine had been the teacher that instructs and the ray that guides and the help in need.

I am greatly indebted to Dr. Eman Salah El-Din Khaliel Lecturer of internal Medicine Medical Research Institute, who has created the idea of the work, and for supervising the whole work and for her effort .

My sincere thanks and gratitude are expressed to Prof. Dr. Mona H. Kandil Professor of chemical pathology Medical Research Institute for her kind cooperation, patience, support and helpful suggestions to accomplish this work.

Finally, I want to express my gratitude and deepest thanks to my family for their moral support.

CONTENTS

Introduction

INTRODUCTION

Diabetes mellitus

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the ß- cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The basis of the abnormalities of carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia. [1]

Classification of diabetes mellitus. [2]

*** Clinical diabetes**

I- Type 1 diabetes, formerly called insulin-dependent diabetes mellitus (IDDM) or "juvenile –onset diabetes"

A-immune mediated

B-idiopathic

II- Type 2 diabetes formerly called non-insulin-dependent diabetes mellitus (NIDDM) or "Adult-onset diabetes"

III- Other specific types

A. Genetic defect of B cell function (e.g. maturity-onset diabetes of the young (MODY)types 1-3 and point mutations in mitochondrial (DNA)

B. Genetic defect in insulin action

C. Disease of exocrine pancreas (e.g. pancreatitis, truma, pancreatectomy, neoplasia, cysticfibrosis, hemochromatosis, fibrocalculous, pancreatopathy)

D. Endocrinopathies (e.g. acromegaly, cushing's syndrome, hyperthyroidism, pheochromocytoma, glucagonoma, somatostinoma, aldosteronoma)

E. Drug or chemical induced (e.g., glucocorticosteroids, thiazides, diazoxide, thyroid hormone, phenytion, B-agonists, oral contraceptives)

F. Infections (e.g., congenital rubella, cytomegalo-virus.)

G. Uncommon forms of immune-mediated diabetes (e.g., 'stiff-man' syndrome, anti- insulin receptor antibodies)

H. Other genetic syndromes (e.g., Down, Klinefelter's, Turner's syndrome)

IV-Gestational diabetes mellitus

* Risk categories

I- Impaired fasting glucose.

II- Impaired glucose tolerance.

Long-term complications of diabetes:

1-Microvascular complications:

Microvascular. complications of diabetes, such as retinopathy, neuropathy, and nephropathy[3].

Diabetic retinopathy is a specific complication of diabetes due to microangiopathy of diabetes. The prevalence of diabetic retinopathy range from 30% to 45% depending on the method of retinal assessment. It occurs after 15 to 20 years in 80% of patients with poorly controlled type 1 or type 2 diabetes[4].

Diabetic neuropathy is a relatively early and common complication affecting approximately 30% of diabetic patients, may be somatic or autonomic. Nearly all patients have grossly abnormal autonomic function tests and about more than half of the patients with advanced nephropathy had symptoms of autonomic neuropathy [5].

Diabetic nephropathy is an important cause of morbidity and mortality, and is now among the most common cause of end-stage renal diseases (ESRD) in developed countries, other types of renal disease are also more prevalent in diabetes. Asymptomatic bacteriuria and pyelonepheritis are about twice as common especially in women. Papillary necrosis is a complication of late stage diabetic disease and is usually seen with clinically and pathologically evident diabetic nephropathy [6].

II- Macrovascular complications :

The clinical manifestations of macrovascular disease are consequences of atherosclerosis of coronary, cerebral, and large arteries of the lower extremities resulting in angina, stroke, and intermittent claudication, respectively[7].

Diabetic nephropathy

(DN) is a major complications of diabetes, which affects up to a half of diabetics worldwide. It accounts for 10-30% of the causes of the end stage renal disease (ESRD) in Africa, while its contribution even higher in more developed countries, reaching almost 50% in the united states[8].

It has now become obvious that type 2 diabetes must be taken seriously as type 1 diabetes, in part because of its renal complication [9].

In the past two decades there was a continual increase in the silence of end-stage renal disease among patients with diabetes, predominantly those with type 2 diabetes.[10]

This is due to the facts that:

1) Diabetes, particularly type 2 is increasing in prevalence.

2) Diabetic patients now live longer.

3) Patients with diabetic ESRD are now being accepted for treatment in ESRD programs where formerly they had excluded .

Diabetic nephropathy is a clinical syndrome characterized by persistent overt albuminuria (> 300 mg / 24 h or > 200 µg /min), a relentless decline in glomerular filtration rate (GFR) and raised arterial blood pressure [11].