

**Tumor necrosis factor alpha (TNF-) as a
predictor of microangiopathy in patients
with type I diabetes mellitus**

Thesis

*Submitted for partial fulfillment of
Master Degree in Pediatrics*

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Introduction :

Diabetes Mellitus :-is a syndrome of disturbed energy homeostasis caused by deficiency of insulin or of its action and resulting in abnormal metabolism of carbohydrate, protein and fat. Diabetes is characterized by long-term complications including nephropathy, retinopathy and neuropathy, all of which are closely related to vascular damage.

(*Martinez, et al.,*)

Well controlled diabetes prevents the occurrence of microvascular complications. (*DCCT research group,*)

Microangiopathy is widely considered a chronic inflammatory disease and Diabetes Mellitus is an important risk factor for occurrence. Inflammatory activity in individuals with Type I Diabetes Mellitus may be due to hyperglycemia and formation of glycation end product.

(*Stamler et al.,*)

Progressive vascular disease is characteristic of Diabetes Mellitus. Microvascular complications of Diabetes Mellitus have complex pathogenesis involving dysfunction and damage to vascular endothelial cells. Vascular endothelial cells are sensitive to stimulatory factors such as hyperglycemia , oxidative stress and advanced glycation endproduct .Association between inflammatory activity and endothelial dysfunction thought to play important role to develop Microvascular complications of Type I Diabetes Mellitus. (*Sernau T et al.,*)

It is well known that type I Diabetes Mellitus is a T-cell dependant autoimmune disease result in selective destruction of beta cell of Langerhans with subsequent programmed cell death i.e. Apoptosis. Tumor necrosis factor-alpha (TNF-) is involved in apoptotic pathways that are implicated in beta cell destruction. (*Ratter et al.,*)

The Aim of the Work :-

To estimate tumor necrosis factor-alpha (TNF- α) in type I diabetes mellitus patients with and without microvascular complications and to evaluate if it has any relation to glycemic control .

Methods:-

Fifty () type I diabetic patients and twenty –five () healthy individuals as controls .

The participant will be divided into groups :

- **Group** : healthy individuals of comparable age and sex as control group
- **Group** : patients with type I Diabetes Mellitus with duration of disease less than years
- **Group** : patients with type I Diabetes Mellitus with duration of disease more than years

All patients and controls will be subjected to laying stress on duration of Diabetes, history of any symptoms suggestive of complication, method of intake of insulin and full clinical examination including BP and fundus examination will be done.

And the following parameters will be evaluated :

- lipid profile including TG, cholesterol , HDL&LDL
- glycosylated Hemoglobin.
- Serum creatinine & BUN
- Micro Albuminuria
- Plasma Tumor necrosis factor alfa by ELISA.

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List of contents

	<i>Page</i>
<i>List of abbreviations</i>	
<i>List of tables</i>	
<i>List of figures</i>	
<i>Introduction and aim of the work.....</i>	
<i>Review of literature</i>	
<i>Tumor necrosis factor</i>	
<i>Subject and methods</i>	
<i>Results</i>	
<i>Discussion</i>	
<i>Summary and conclusion</i>	
<i>Recommendations</i>	
<i>Appendix</i>	
<i>References</i>	
<i>Arabic summary</i>	

List of abbreviations

<i>ACE</i>	Angiotensin converting enzyme
<i>CAN</i>	Cardiovascular autonomic neuropathy
<i>DAISY</i>	Diabetes autoimmunity study in the young
<i>DCCT</i>	Diabetes Control and Complications Trial
<i>DKA</i>	Diabetic ketoacidosis
<i>DM</i>	Diabetes mellitus
<i>GAD</i>	glutamic acid decarboxylase
<i>GBM</i>	Glomerular basement membrane
<i>GFR</i>	glomerular filtration rate
<i>HAAF</i>	hypoglycemia-associated autonomic failure
<i>HbA_c</i>	glycosylated hemoglobin
<i>HLA</i>	Human leukocyte antigen
<i>HPLC</i>	high performance liquid chromatography
<i>IDF</i>	International Diabetes Federation
<i>IFG</i>	Impaired fasting glucose
<i>IGT</i>	Impaired glucose tolerance
<i>IRS-</i>	insulin receptor substrate-
<i>NPDR</i>	Non-proliferative diabetic retinopathy
<i>PAI-</i>	plasminogen activator inhibitor-
<i>PDR</i>	Proliferative diabetic retinopathy
<i>SCII</i>	Continuous subcutaneous insulin infusion
<i>SMBG</i>	Self monitoring blood glucose
<i>STATS</i>	signal transducers and activators of transcription
<i>TNF-</i>	Tumor necrosis factor alpha

VCAM-	vascular cell adhesion molecule-
VEGF	vascular endothelial growth factor
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy

	<i>List of tables</i>	<i>Page</i>
Table ()	Etiologic classification of diabetes	
Table ()	The incidence and prevalence rate of type diabetes mellitus in different countries	
Table ()	The American Diabetes Association guidelines for the evaluation of glucose level ()	
Table ()	Stages of diabetic nephropathy	
Table ()	Good glycemic control reduces incidence of complications	
Table ()	Comparison of human insulin and insulin analogues	
Table ()	Plasma Blood Glucose and HBA c Goals for Type Diabetes by Age Group	
Table ()	Comparison of age, sex, duration of disease and biochemical parameter between type diabetic patients with and without microvascular diabetic complication complications versus control subjects	
Table ()	Comparison between control group and all patients group	
Table ()	comparison between group A (more than years duration of disease) and group B (years duration of disease or less)	
Table ()	comparison between patients with microvascular complications and patients without microvascular complication	
Table ()	Correlation between age, duration and biochemical parameters in complicated patients.	

Table ()	Correlation between age, duration and biochemical parameters in uncomplicated patients .	
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	<i>List of figures</i>	<i>Page</i>
<i>Figure()</i>	Incidence of diabetes mellitus in children aged from - years worldwide	
<i>Figure()</i>	Hypothetical stages and loss of beta cells in an individual progressing to type A diabetes	
<i>Figure()</i>	Progression to diabetes of first degree relatives of patients with type diabetes subdivided by the number of autoantibodies expressed (of GAD , ICA , and insulin)	
<i>Figure()</i>	The relationship between the Grade of Consciousness and plasma osmolarity (mOsm/liter, calculated) in patients with diabetic ketoacidosis.	
<i>Figure()</i>	Hypoglycemia associated autonomic failure	
<i>Figure()</i>	Classification of polyneuropathy	
<i>Figure()</i>	Signal transduction by TNF receptors	
<i>Figure()</i>	Functions of cytokines in host defense	
<i>Figure()</i>	percentage of patients with and without microvascular diabetic complications	
<i>Figure()</i>	Comparison study between patients with microvascular complications and patients without microvascular complications	
<i>Figure()</i>	Comparison study between mean value of serum TNF- in the various studied groups	
<i>Figure()</i>	Comparison study between mean value of HBA c in the various studied groups .	

Intorduction

and aim of

the work

List of contents

	<i>Page</i>
<i>List of abbreviations</i>	<i>II</i>
<i>List of tables</i>	<i>III</i>
<i>List of figures</i>	<i>IV</i>
<i>Introduction and aim of the work</i>	<i>۱</i>
<i>Review of literature</i>	
▪ <i>Diabetes mellitus</i>	<i>۳</i>
▪ <i>Tumor necrosis factor</i>	<i>۴۲</i>
<i>Subject and methods</i>	<i>۵۳</i>
<i>Results</i>	<i>۵۹</i>
<i>Discussion</i>	<i>۶۸</i>
<i>Summary and conclusion</i>	<i>۷۶</i>
<i>Recommendations</i>	<i>۷۸</i>
<i>Appendix</i>	<i>۷۹</i>
<i>References</i>	<i>۸۴</i>

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<i>IRS-¹</i>	insulin receptor substrate- ¹
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<i>PDR</i>	Proliferative diabetic retinopathy
<i>SCII</i>	Continuous subcutaneous insulin infusion
<i>SMBG</i>	Self monitoring blood glucose
<i>STATS</i>	signal transducers and activators of transcription
<i>TNF-α</i>	Tumor necrosis factor alpha
<i>UAE</i>	Urinary albumin excretion
<i>VCAM-¹</i>	vascular cell adhesion molecule- ¹
<i>VEGF</i>	vascular endothelial growth factor
<i>WESDR</i>	Wisconsin Epidemiologic Study of Diabetic Retinopathy

	<i>List of tables</i>	<i>Page</i>
Table (١)	Etiologic classification of diabetes	٤
Table (٢)	The incidence and prevalence rate of type ١ diabetes mellitus in different countries	٧
Table (٣)	The American Diabetes Association guidelines for the evaluation of glucose level (٢٠٠٣)	١٦
Table (٤)	Stages of diabetic nephropathy	٢٧
Table (٥)	Good glycemic control reduces incidence of complications	٣٥
Table (٦)	Comparison of human insulin and insulin analogues	٣٧
Table (٧)	Plasma Blood Glucose and HBA ^١ c Goals for Type ١ Diabetes by Age Group	٤١
Table (٨)	Comparison of age, sex, duration of disease and biochemical parameter between type ١ diabetic patients with and without microvascular diabetic complication complications versus control subjects	٥٩
Table (٩)	Comparison between control group and all patients group	٦٠
Table (١٠)	comparison between group A (more than ٥ years duration of disease) and group B (٥ years duration of disease or less)	٦١
Table (١١)	comparison between patients with microvascular complications and patients without microvascular complication	٦٢
Table (١٢)	Correlation between age, duration and biochemical parameters in complicated patients.	٦٣
Table (١٣)	Correlation between age, duration and biochemical parameters in uncomplicated patients .	٦٤

	<i>List of figures</i>	<i>Page</i>
<i>Figure(١)</i>	Incidence of diabetes mellitus in children aged from ٠-١٤ years worldwide	٨
<i>Figure(٢)</i>	Hypothetical stages and loss of beta cells in an individual progressing to type ١A diabetes	٩
<i>Figure(٣)</i>	Progression to diabetes of first degree relatives of patients with type ١ diabetes subdivided by the number of autoantibodies expressed (of GAD٦٥, ICA٥١٢, and insulin)	١٤
<i>Figure(٤)</i>	The relationship between the Grade of Consciousness and plasma osmolarity (mosm/liter, calculated) in ٧٠ patients with diabetic ketoacidosis.	١٩
<i>Figure(٥)</i>	Hypoglycemia associated autonomic failure	٢٢
<i>Figure(٦)</i>	Classification of polyneuropathy	٣١
<i>Figure(٧)</i>	Signal transduction by TNF receptors	٤٣
<i>Figure(٨)</i>	Functions of cytokines in host defense	٤٦
<i>Figure(٩)</i>	percentage of patients with and without microvascular diabetic complications	٦٥
<i>Figure(١٠)</i>	Comparison study between patients with microvascular complications and patients without microvascular complications	٦٦
<i>Figure(١١)</i>	Comparison study between mean value of serum TNF- α in the various studied groups	٦٧
<i>Figure(١٢)</i>	Comparison study between mean value of HBA١c in the various studied groups .	٦٧

Introduction

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