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

Thesis

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Master Degree in Pediatrics
By

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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.,*** ١٩٩٦***)***

Well controlled diabetes prevents the occurrence of microvascular complications. ***(DCCT research group,*** ١٩٩٣***)***

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.,*** ١٩٩٣***)***

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 Microvacular complications of Type I Diabetes Mellitus. ***(Sernau T et al.,***١٩٩٥***)***

It is well known that type I Diabetes Mellitus is a T-cell dependant autoimmune disease result in selective destruction of beta cell of Largerhans with subsequent programmed cell death i.e. Apoptosis. Tumor necrosis factor-alpha (TNF-α) is involved in apoptotic pathways that are implicated in beta cell destruction. ***(Ratter et al,.***١٩٩٩***)***

The Aim of the Work :-

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

Methods:-

Fifty (٥٠) type I diabetic patients and twenty –five (٢٥) healthy individuals as controls .

The participant will be divided into ٣ groups :

- ***Group I*** :٢٥ healthy individuals of comparable age and sex as control group

- ***Group Ц***:٢٥ patients with type I Diabetes Mellitus with duration of disease less than ٥ years

- ***Group Ш***: ٢٥ patients with type |I Diabetes Mellitus with duration of disease more than ٥ 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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Also, I thank our patients who permitted me to do my study, and I hope to give them benefit and improve their quality of life.

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List of abbreviations

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

VCAM-١	vascular cell adhesion molecule-١
VEGF	vascular endothelial growth factor
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy

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Intorduction and aim of the work

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HbA١c	glycosylated hemoglobin
HLA	Human leukocyte antigen
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