Egyptian Society of Diabetes and Lipidology Journal

ESDL Journal

ESDL Chairman

Prof. Mohamed Khattab

Board Members (In Alphabetical Order)

Prof. Atef Bassiouny	*Prof. Nermine Sheriba*
Prof. Hesham El Gayar	*Prof. Salah Shelbaya*
Prof. Ibrahim Elebrashy	*Prof. Samir George*
Prof. Khalifa Abdallah	*Prof. Sherif Hafez*
Prof. Mohamed Khattab	*Prof. Yehia Ghanem*
Prof. Nabil El Kafrawy	

About the Journal

ESDL Journal is an open access peer-reviewed journal that publishes high quality materials on all aspects of diabetes mellitus and lipidology, its complications and related relevant topics. Our Journal is dedicated to provide updated information to junior doctors in the form of review articles, abstracts, and case studies. It also provides a forum for exchange of information in all fields of diabetes and lipidology.

Editor in Chief:

Prof. Nabil Elkafrawy

Editorial office:

ICOM
North Africa Offices:
- Alexandria: El Asdekaa building (2)– Masged El Asdekaa st., Garden City Smouha-Egypt
- Cairo: 17 Emarat El Madfaeya, City Stars st., infront of Masged El Kowat El Mosalaha, Nasr City – Egypt
TEL./Fax: +2034204849 / +2034249072 Cellular: +201001224849 +201208000270

***Gulf Offices*:**
-Dubai: Damac Business tower 1, El Abraj st, Business Bay, Burj Khalifa Community- Office 1003- Dubai TEL.: +097144307892
-Manama: TEL.: +973 336 62 996
Email: info@icomgroup.org

Content

SECTION (1): ABSTRACTS PRESENTED @ DIAEGYPT

Effect of Short-Term Erythropoietin Therapy on Insulin Resistance in Diabetic and Non-Diabetic Hemodialysis Patients

Mai A.Kamel [1](MD), Walid A.Shehab-Eldin[1] (MD), Heba E. Kasem[1] (MD), Islam S. Shebl[2] MB BCh, Ahmed A. Sonbol[3] (MD)*

OBJECTIVE

Insulin resistance (IR) is a frequent multifactorial complication of uremia. It is considered an independent predictor for cardiovascular events and mortality in patients with chronic kidney disease (CKD); it may be an important therapeutic target in management of CKD. The study was conducted to evaluate the effect of short-term treatment with recombinant human erythropoietin (rHuEpo) therapy on IR, in diabetic and non-diabetic end stage renal disease (ESRD) patients on hemodialysis.

METHODS

A prospective study of 60 ESRD patients on regular hemodialysis subdivided into two groups; Group I (n=30) non-diabetic patients on regular hemodialysis and Group II (n=36) diabetic patients on regular hemodialysis both group received subcutaneous (rHuEpo) in a dose os 80-120 u/kg/week for 6 months. HOMA-IR used to calculate IR after 6 months of (rHuEpo) therapy.

RESULTS

IR was significantly higher in group II than group I; HOMA-IR of group I and II was 1.64±0.88 and 10.78±2.84 respectively ($p<0.001$). On comparing results before and after (rHuEpo) therapy in both groups there was significant improvement in IR. HOMA-IR was 1.64±0.88 and 0.8±0.28 ($p<0.001$) before and after intervention for G I while it was 10.78±2.84 and 5.52±161 ($p<0.001$) before and after intervention for G II. HbA1C, total cholesterol as well as fasting and postprandial glucose measurements showed significant improvement in both groups on comparing results before and after (rHuEpo) therapy

CONCLUSION

IR is improved by (rHuEpo) therapy in hemodialysis diabetic as well as non-diabetic patients.

KEYWORDS

End-Stage Renal Disease, Hemodialysis, Erythropoietin, Diabetes Miletus, Insulin Resistance.

---

[1]Internal Medicine, Faculty of medicine, Menoufia University, Menoufia, Egypt

[2]Department of Nephrology, Shibin El-Kom Teaching Hospital, Menoufia, Egypt

[3]Clinical pathology, Faculty of medicine, Menoufia University, Menoufia, Egypt

Is Endothelial Dysfunction the Main Issuse in Prediabetic as Predictor for Cardiovascular Diseases

Salam RF[1], Wadie M[2]*

BACKGROUND

The frequency of prediabetes is increasing as the prevalence of obesity rises worldwide. Hyperglycemia, insulin resistance, inflammation and metabolic derangements associated with concomitant obesity cause endothelial dysfunction in prediabetics, leading to increased risk of cardiovascular and renal disease.

OBJECTIVE

To get a general perspective on the complex relationship between cardiovascular diseases onset, and pre-doiabetes

METHODOLOGY

100 obese patients compared to 45 normal controls the study was conducted between June 2018 and April 2018. All subjects were submitted to history taking, clinical examination including wasit circumference, BMI, Hb A1c, Fasting blood glucose, lipid profile, carotid artery duplex, and Brachial artery flow media dilation (FMD)

RESULTS

Mean age of our patients was 30±0.3 years, cholesterol was 240±22.1mg/dl, triglycerides was 105±12.2 mg/dl, LDL was140.7±32.1 mg/dl, HDL was 38.45±9.5 mg/dl, and A1C mean 5.95±0.2

There was statistically significant difference in Carotid intimal media thickness between prediabetic and controls (P <0.01). However, there was no statistical significance difference between patient and control regarding FMD (p ;0.26)

CONCLUSION

screening for prediabetes is of utmost importance for prevention of cardiovascular morbidity as it is an incipient for premature atherosclerosis, endothelial dysfunction follow changes in CIMT, which highlights that screening of CVS in prediabetics should be done by CIMT and not by FMD

1,2 Department of Internal Medicine, Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University, Cairo, EGYPT.

NLRP3 Inflammasome Expression and Urinary HSP72 In Relation to Biomarkers of Inflammation and Oxidative Stress in Diabetic Nephropathy Patients

*Yasser M.Hafez**, Hemat El-Sayed El-Horany , Rania Nagi Abd-ELlatif , Mona Watany , Hanaa Ibrahim Okda*

BACKGROUND:

Diabetic nephropathy (DN) is one of the major causes of end-stage renal disease. Nod-like receptors nucleotide-binding domain and leucine-rich repeat pyrin-3 domain (NLRP3 (inflammasome displays a considerable role in the chronic inflammatory state observed in diabetic patients. Urinary heat shock protein 72 (uHSP72) is a sensitive and specific biomarker for the early detection the acute kidney injury. The aim of this study was to evaluate NLRP3 relative gene expression, its correlation with inflammatory and oxidative stress markers, and to assess the value of uHSP72 in the early detection of DN in type 2 diabetic patients with different degrees of DN. Forty-five type 2 diabetic patients were enrolled in this study: 15 normoalbuminuric; 15 microalbuminuric; 15 macroalbuminuric patients in addition to 15 healthy controls. Clinical examination and routine laboratory investigations were done. NLRP3 mRNA expression was assessed by real time PCR. Serum 8-hydroxy-2'-deoxyguanosine (8-OHdG), IL-1β and uHSP72 levels were estimated by enzyme-linked immunosorbent assay. Serum chitotriosidase (CHIT1) activity was examined. Significant higher NLRP3 mRNA expression ,serum 8-OHdG, IL-1β and uHSP72 levels, in addition to CHIT 1 activity were documented in the macroalbuminuric patient group as compared to the other two diabetic and control groups. They were significantly positively correlated and to urinary albumin/creatinine ratio, serum creatinine and HA1c. Multiple linear regression analysis using UACR as dependent variable ,confirmed that uHSP72, and relative NLRP3 mRNA expression were the independent predictors of DN (β were 0.432 and 0.448 respectively, P<0.001). Receiver operating characteristic analyses revealed that both NLRP3 mRNA expression and uHSP72 levels were useful biomarkers discriminating DN patients from T2DM patients (AUC were 0.957 and 0.983 respectively)

CONCLUSION:

uHSP72 may be considered as a novel potential diagnostic biomarker for the early detection of DN. Moreover, these data support the pivotal role of NLRP3 in the development and progression of DN.

---

*lecturer of internal medicine, Diabetes and Endocrinology unit. Faculty of Medicine, Tanta University, Egypt.

Role of Inflammatory Markers in Elderly Type 2 Diabetic Patients with Mild Cognitive Impairment

Salwa S. Hosny[1], Ahmed M. Bahaaeldin[1], Mohamed S. Khater[2], Meram M. Bekhet[1]

ABSTRACT

Type 2 diabetes (T2DM) is a risk factor for Alzheimer's disease and mild cognitive impairment. The etiology of cognitive impairment in people with T2DM is uncertain but, chronic hyperglycemia, cerebral micro vascular disease, severe hypoglycemia, and increased prevalence of macro vascular disease are implicated

INTRODUCTION

Mild Cognitive Impairment (MCI) represents the intermediate stage between normal ageing and dementia. Patients with MCI have an increased risk of developing dementia, with an estimated annual conversion rate to dementia of 12% [1]. The various causes of MCI include neuro degenerative diseases, such as Alzheimer's disease, cerebrovascular disease, major psychiatric illnesses like depression, and other systemic causes [2]. Type 2 diabetes (T2DM) is a risk factor for Alzheimer's disease and mild cognitive impairment. The aetiology of cognitive impairment in people with T2DM is uncertain, but it is most likely multifactorial. Chronic hyperglycaemia, severe hypoglycaemia, and increased prevalence of macro vascular disease have all been implicated but are unlikely to explain the entire effect [3]. T2DM is associated with atherosclerosis of the cerebral arteries and leads to important cerebral vascular changes that cause a decrease in cerebral blood flow. Furthermore, hyperglycemia is accompanied by an accelerated rate of advanced glycation end product (AGE) formation, which is associated with increased amyloid deposition and oxidative stress which all lead to developing of cognitive impairment [4]. One of the theories is that endothelial activation or inflammatory processes may be involved in the pathogenesis of MCI in diabetes [5].

OBJECTIVE

The aim of the study is to determine the serum levels of soluble vascular adhesion molecule (sVCAM-1) and highly sensitive C- reactive protein (Hs-CRP) in elderly T2DM with mild cognitive impairment (MCI).

RESULTS

Serum levels of sVCAM-1 in diabetic elderly patients with MCI were significantly higher (946.7 ± 162.01 ng/ml) than diabetic elderly patients without cognitive impairment (479.06 ± 65.27 ng/ml) and control (263.7 ± 72.05 ng/ml) with (P=0.002). Serum levels of Hs-CRP in diabetic elderly patients with MCI were significantly higher than as diabetic elderly patients without cognitive impairment and control with (P=0.005).

	Group I		Group II		Group III		All Diabetic	
	R	P-value	r	P-value	r	P-value	r	P-value
Age (years)	-0.12	0.205	-0.247	0.094	0.198	0.147	-0.215	0.050
Wt (Kg)	-0.164	0.127	-0.063	0.371	0.486	0.003	-0.434	0.000
BMI (Kg/m2)	-0.250*	0.04	-0.049	0.398	0.395*	0.015	-0.387	0.001
SBP (mmHg)	-0.025	0.437	0.000	0.5	-0.009	0.482	0.034	0.399
DBP (mmHg)	0.062	0.353	0.000	0.5	-0.085	0.328	0.000	0.500
Years of education (years)	-0.157	0.142	-0.394*	0.016	-0.141	0.229	-0.017	0.448
T.G(mg/dl)	-0.08	0.288	0.165	0.191	0.216	0.125	0.435**	0.000
T.C(mg/dl)	-0.064	0.327	0.187	0.161	-0.121	0.261	0.507**	0.000
HDL(mg/dl)	-0.075	0.3	0.22	0.122	0.006	0.488	-0.094	0.238
LDL(mg/dl)	0.161	0.128	-0.019	0.461	0.251	0.090	0.366**	0.002
FPG (mg/dl)	0.123	0.199	-0.113	0.276	-0.070	0.357	0.195	0.068
2PPPG(mg/dl)	0.329*	0.011	-0.143	0.225	-0.105	0.291	0.242	0.031
HbA1c%	0.519**	0.000	-0.213	0.129	-0.102	0.296	0.494**	0.000
Pr/Cr(mg/dl)	0.466**	0.001	-0.066	0.365	-0.043	0.410	0.369**	0.002
SVCAM-1(ng/ml)	0.725**	0.000	0.525**	0.001	0.094	0.311	0.912**	0.000

**P-value < 0.01 is high statistical significant

*P-value < 0.05 is significant

	Group I		Group II		Group III		All Diabetic	
	R	P-value	R	P-value	R	P-value	R	P-value
Age (years)	-0.017	0.45	-0.258	0.084	0.038	0.421	-0.224	0.043
Wt (Kg)	-0.272*	0.019	0.106	0.288	0.169	0.186	-0.554	0.000
BMI (Kg/m2)	-0.256*	0.028	-0.316*	0.044	0.157	0.204	-0.467	0.000
SBP (mmHg)	0.095	0.254	0.096	0.306	0.115	0.273	0.090	0.247
DBP (mmHg)	0.127	0.199	0.054	0.388	0.006	0.487	0.048	0.357
Years of education (years)	-0.099	0.23	-0.618**	0.000	-0.250	0.091	0.005	0.485
T.G(mg/dl)	-0.018	0.443	-0.03	0.437	0.306	0.050	0.439**	0.000
T.C(mg/dl)	-0.149	0.126	0.199	0.145	-0.008	0.483	0.497**	0.000
HDL(mg/dl)	0.049	0.354	0.360*	0.026	-0.038	0.422	-0.061	0.322
LDL(mg/dl)	0.099	0.221	0.396*	0.018	0.098	0.303	0.319**	0.007
FPG (mg/dl)	0.249*	0.031	-0.091	0.316	0.583	0.130	0.331**	0.005
2PPPG(mg/dl)	0.259*	0.024	-0.279	0.068	0.545	0.115	0.335**	0.004
HbA1c%	0.501**	0.000	0.054	0.389	0.635	0.210	0.614**	0.000
Pr/Cr(mg/dl)	0.293*	0.013	-0.252	0.089	0.490	0.101	0.474**	0.000
HsCRP(ng/ml)	0.725**	0.000	0.525**	0.001	0.094	0.311	0.912**	0.000

**P-value < 0.01 is high statistical significant

*P-value < 0.05 is significant

Correlation between HsCRP and all studied parameters in all groups..

Correlation between SVCAM-1 and all studied parameters in all groups.

CONCLUSION

Elderly diabetic patients with mild cognitive impairment have higher levels of soluble adhesion molecules and markers of low-grade systemic inflammation than other groups.

REFERENCE:

[1] Petersen RC. Mild cognitive impairment. The New England Journal of Medicine, 2011; 364(23): 2227–2234. [2] Plassman Bl, Langa KM, Fisher GG, et al. Prevalence of cognitive impairment without dementia in the United States. Annals of Internal Medicine, 2008; 148: 427–434. [3] Strachan MW, Reynolds RM, Marioni RE, Price JF. Cognitive function, dementia and type 2 diabetes mellitus in the elderly. Nature Reviews Endocrinology, 2011; 7(2): 108–114. [4] Kumar V, Fausto N, Abbas AK, Aster JC. Robbins and Cotran Pathologic Basis of Disease, 2015. [5] Hermida AP, McDonald WM, Steenland K, Levey A. "The association between late-life depression, mild cognitive impairment and dementia: Expert Review of Neuro therapeutics, 2012; 12(11): 1339–1350

---

[1]Department of Internal Medicine, and Endocrinology,

[2]Department of Geriatric Medicine, Faculty of Medicine, Ain Shams University

Severe Hypertriglyceridemia in Type 1 Diabetes Accompanied by Acute Pancreatitis and Organomegaly

Ibrahim Elebrashy, Hemmat E. El Haddad, Ahmed Rabie, Mona Yousry Helmy, Maha Youssef Rakha, Randa F Salam

INTRODUCTION:

Severe HTG usually occurs in a patient with genetic predisposition and exacerbated by secondary factors as diabetes, obesity, high alcohol intake or adverse effect of medication.

CASE REPORT:

21yr old female patient visited the emergency department with repeated attacks of vomiting accompanied with continuous non radiating epigastric pain diagnosed as acute pancreatitis. She had three plasmapheresis sessions

The patient gave history of recurrent similar attacks for the last 5 years with frequent hospitalization she is known diabetic since the age of 15.Hypertensive for 1 year .Menarche at age of 14 with only one cycle

Upon admission, the patient was alert ,Weight: 60 kg , Height : 164 cm. BMI: 22 Pulse: 90 beat /minute Blood pressure: 130/70 Respiratory rate: 14 /minute. Temperature: 37ºC Physical examination: Eruptive xanthoma on the extensor surface of the forearms & back.

Cardiac examination: apex localized in the left fifth space outside MCL, hyper dynamic. Hepatomegaly 2 fingers below RT costal, normal fundus, normal neurological examination Breast: Tanner 3, Pubic hair: Tanner 4 Laboratory investigations; RBS 375mg/dl HBA1C: 14.7 %, ABG (PH: 7.38 HCO3: 26 Mm/L SaO2 98.0%)

CBC HB;11.6 g/dl , TLC: 5.800/uL PLT:245,000/uL / CRP: 132mg/dl /Chol : 464mg/dl ,LDL: 257 mg/dl ,HDL: 25 mg/dl , TG: 9068 mg/dl Amylase: 1120U/L, Lipase : 370U/L/Na: 141mEq/L, K: 3.8 mEq/L, Urea :34mg/dl Creatinine:5mg/dl ,24 hrs. Urinary PTN : 1.146 gm. ALT: 17 IU/L, AST: 19IU/L ,Bil T: 0 .9mg/dl ,Albumin : 4 g/dl FSH:0.1,LH:0.5 ,Estradiol :5,TSH:1.7 ,FT4 :1,ACTH:12 ,Cortisol AM:8,GH:0.1ng/ml Abdominopelvic sonar showed: Enlarged Bright hepatomegaly 16 cms ,Mild splenomegaly. Diffuse enlarged pancreas of hypo echoic pattern, picture suggestive of acute pancreatitis. Enlarged swollen kidneys (RT kidney 154*48mm, LT kidney 152*75mm.) CT abdomen with contrast: Diffusely enlarged pancreatic head X-ray both arms: Bilateral distal humorous multiloculate bubbly lesion with sclerotic margin Echocardiography: Concentric LT ventricular hypertrophy .MRI brain (Bulky pituitary gland showing a focal central bulge (0.4x 1x0.7).

Renal biopsy: Minimal change glomerulonephritis.

After three plasmapheresis sessions, Intravenous insulin a marked reduction in triglyceride /total cholesterol levels was observed. CHOL 334mg/dl, LDL 190mg/dl, HDL 48mg/dl, TG 880mg/dl

She was discharged on dietary, lifestyle modifications and fenofibrates 4 month later she came for follow up Marked improvement of her xanthomata, regular cycles, TG 627mg/dl, HbA1c :8.9,normal pituitary imaging,no organomegaly

CONCLUSION:

Patients with severe hypertricylcerideamia require fast and effective lowering of TG levels in order to reverse the lipotoxic effect on different organs

KEYWORDS

hypertriglyceridemia; plasmapheresis; organomegaly,lipotoxicity

---

Internal Medicine, Endocrinology and diabetes Cairo university

ESDL Journal Volume (1) Issue (1)

Statins Induced Myopathy Among Diabetes with Peripheral Neuropathy: Incidence, Etiology and Management

Randa Kozman, Alyâa Ramadan

OBJECTIVE

Statins induced myopathy and neuropathy are more pronounced in diabetes suffering from peripheral neuropathy. Lipid lowering drugs are indispensable for cardiovascular protection in diabetes. Myopathy is principal reason for statins non adherence and /or discontinuation. This study aims to answer what is the rate of incidence does statin undesirable effects myopathy affecting diabetes especially those with complication as neuropathy which aggravates it, etiology and best management (and alternatives) to profit statins benefits overcoming its risks.

METHODS AND RESULTS

In Cohort study, researchers identified patients age, sex, risk factors, cardiac status, laboratory analysis used patients case records to define all clinical courses of statin induced myopathy. Diabetes suffered from peripheral neuropathy complication used statins for cardiovascular protection who most of them complained from statins induced myopathy (muscles related symptoms).

Incidence of myopathy among diabetes with peripheral neuropathy was found =67.77%

Diabetes suffered from statins myopathy were 65%, among them 81% discontinued statin therapy as couldn't tolerate myopathy ...where, those tolerated myopathy were 35%.

Patients stopped statins were shifted to another statin where 68% of them experienced recurrent muscle pain, and 32% tolerated other statin without recurrent muscle symptoms. 3patients were hospitalised for rhabdomyolysis management, one was sent to ICU. 1 patient with preexisting renal insufficiency began lifelong dialysis. Neuropathy pain is difficult to distinguish from statin or from diabetes complication. In one study, 26% over 65 years old develop peripheral neuropathy in life (without any known risk factor). That's third cause of those patients complaining from neuropathy.

CONCLUSION

Diabetes with peripheral neuropathy have 1.69 times higher risk to develop statin associated myopathy than diabetes without peripheral neuropathy.

Combination of statin and non-statin lipid lipid lowering drug such as ezetimibe is recommended as it allows clinicians to decrease statin doses for patients while reaching LDL-C reduction and therapeutic goals. Also, Pharmacoeconomic benefits of cost effectiveness and clinical utility are gained. Rechallenge of recurrent myopathy when shifted to another statin, to overcome more hydrophillic statins are recommended as pravastatin, rosuvastatin and fluvastatin. Statin choice must be guided by pharmacogenetic patient study, which influences drug pharmacokinetics and pharmacodynamics. By evaluation of transporter function of OATP1B1 haplotypes, located on hepatocytes where statins are substrates and SLCO1B1gene codes for..myopathy status is define, which is individually evaluated of greatest benefit with dramatically no undesirable effect. That is may be addressed in well-designed ongoing clinical trials.

Clinical pharmacy department, Faculty of pharmacy, Alexandria University

Study of Role of Fetuin-A in Development of Diabetic Foot in Patients with Type 2 Diabetes

Nermin Sheriba[1], Yara Muhammad Eid[1], Ahmed Mohamed Bahaaeldin[1]

INTRODUCTION

Diabetic foot is one of the major complications of diabetes and is the main reason for nontraumatic major amputations. common clinical features of diabetic foot include ulcers, foot deformity, infection, neuropathy, PAD, osteomyelitis, and gangrene. In studies using the ankle-brachial index (ABI), which is the preferred screening technique, the prevalence of PAD (defined as an ABI <0.90) in diabetic individuals ranges from 20% to 30%. The duration and severity of diabetes correlates with the incidence and extent of PAD. In a prospective cohort study (Rundle AG., et al 2005) found a strong positive association between the duration of diabetes and the risk of developing PAD. Serum fetuin-A is a multifunctional glycoprotein, which is exclusively secreted from hepatocytes in humans. An association between insulin resistance and type 2 diabetes in individuals with high serum fetuin-A levels was reported. The role of fetuin-A and its involvement in patients with type 2 diabetes and PAD, who commonly suffer from advanced/systemic atherosclerosis, seems to be very complex and has not been fully understood as yet. Fetuin-A is increased in insulin resistance and it is an independent predictor of type-2 diabetes.Fetuin-A inhibits insulin receptor tyrosine kinase activity by inhibiting the auto phosphorylation of tyrosine kinase and IRS-1(insulin receptor substrate proteins).

AIM OF THE WORK

To investigate the relationship between the presence of different diabetic foot lesions and serum fetuin-A levels.

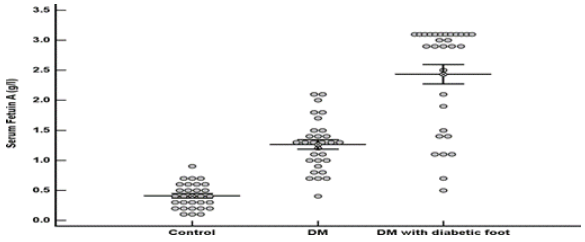
PATIENTS AND METHODS

The study was performed on 30 patients with T2DM having diabetic foot lesions, 30 patients with T2DM without diabetic foot lesions, and 30 healthy subjects as a control. Patients were recruited from the diabetic foot clinics and diabetes outpatient clinics at Ain Shams University hospital after the provision of written informed consent. Laboratory assessments included full lipid profile, glycosylated haemoglobin (HbA1c), fasting blood glucose (FBG), and post prandial blood glucose (PPBG). Serum fetuin-A level was measured using the ELISA technique. Foot assessment was done using the diabetic foot screening and risk stratification form of the Foot Action Group of the Scottish Diabetes Group.

RESULTS

Serum fetuin-A level was significantly higher in patients with diabetic foot (2.43 ± 0.88 g/l) in comparison to diabetic patients without diabetic foot (1.26± 0.43 g/l) with p value < 0.001 and both groups has a significantly higher fetuin-A levels than healthy controls. Both fetuin A and duration of diabetes were independent predictors for the occurrence of diabetic foot.

We found a significant direct correlation between age and serum Fetuin-A levels with p value of 0.0006. Positive significant correlations were also found between serum Fetuin- A level and diastolic blood pressure, HbA1c, triglycerides, and duration of diabetes (p = 0.002, 0.0001, 0.003, 0.027 respectively). The study found also that serum Fetuin-A level was significantly negatively correlated with HDL level with p value of less than 0.0001.



CONCLUSION:

The role of fetuin-A and its involvement in patients with type 2 diabetes and PAD, who commonly suffer from advanced/systemic atherosclerosis, seems to be very complex and has not been fully understood yet. In addition, low fetuin-A might result in vascular calcification and associated with mediasclerosis. So it is clear that only a normal level of fetuin-A is beneficial for humans.

Internal Medicine, Faculty of Medicine, Ain Shams University, Egypt

The Emerging Role of the Epigenetic Enzyme Sirtuin-1 And High Mobility Group Box 1 in Patients with Diabetic Foot Ulceration

Yasser Mostafa Hafez[1], Omnia Safwat El-Deeb[2], Marwa Mohamed Atef[2]

BACKGROUND:

Diabetic foot ulceration (DFU) is a serious diabetic complication that can progress to amputation and since SIRT1 regulates glucose metabolism, inflammation, and oxidative stress which are the major contributors in diabetic complications, so we aimed to discuss its role as an epigenetic biomarker in DFU and highlight its link to oxidative stress and inflammatory cytokines.

METHOD:

60 DM patients were enrolled in the study, 30 without DFU and 30 with DFU in addition to 15 healthy subjects (control group). SIRT1 mRNA relative gene expression was assessed. Catalase activity, advanced glycation end products (AGEs), tumor necrosis factor alpha (TNFα), interleukin 6 (IL-6) and High mobility group box1 (HMGB1) levels were measured. DNA fragmentation was also performed.

RESULT:

SIRT1 expression and catalase activity were significantly decreased in diabetic patients compared to control group with the lowest levels in DFU patients, TNFα, IL-6, HMGB 1 and AGEs levels were significantly higher in the diabetic patients compared to control group with the highest levels in DFU patients. DNA fragmentation was more profound in DFU patients.

CONCLUSION:

The study revealed that SIRT1 mRNA expression can be considered as a novel biomarker in DFU being a major player involved in its pathogenesis.

---

[1]Lecturer of Internal Medicine, Internal Medicine Department, Faculty of Medicine, Tanta University, El Geesh street, Tanta, Egypt
[2]Lecturers of Medical Biochemistry, Medical Biochemistry Department, Faculty of Medicine, Tanta University, El Geesh street, Tanta, Egypt

ESDL Journal Volume (1) Issue (1)

Thyroid Autoimmunity in Type 2 Diabetic Female Patients

Ibrahim El Ebrashy[1], Amr El Meligi[1], Laila Rashed[2], Randa Fayez[1], Elham Youssef[1], Shaimaa Fathy[1]

BACKGROUND:

High prevalence of thyroid disorders is more common in T1 compared to T2 Diabetes Mellitus due to the associated autoimmunity, with hypothyroidism being the most common disorder.

OBJECTIVES:

The aim of this study is to assess the prevalence of thyroid dysfunction among T2 diabetic Egyptian females and to find the correlation between the metabolic syndrome components and autoimmune thyroid dysfunction.

METHODS:

The study included 81 T2 diabetic Egyptian female subjects and 60 sex and aged matched controls. Patients were divided in two age groups (≤ or > 40 years). All patients in the study were subjected to anthropometric measures, HbA1c, lipid profile, serum uric acid, TSH, FT3, FT4, Anti TPO, Anti TG and thyroid ultrasound.

RESULTS:

Hypothyroidism was found in 35.8% of patients (5.17± 3.30µIU/ml) versus 10% of controls (1.77± 1.18µIU/ml) ($p < 0.001$). Anti TPO was found in 52% (323.68± 245.84 IU/ml) of patients versus 5% (29.95± 28.62 IU/ml) of control ($p < 0.001$). Anti TG was found in 40% (476.98 ± 361.15 IU/ml) of patients versus 0% (54.12± 38.20 IU/ml) of control (p value < 0.001). A significant positive correlation was found between antithyroid antibodies (ATG, ATPO) and TSH (P value: 0.002, 0.008 respectively). A significant positive correlation was found between all components of metabolic syndrome and TSH, but not with thyroid antibodies.

CONCLUSION:

Autoimmune thyroid disease is more common in Egyptian women with T2 diabetes than non diabetic women, regardless the age, and therefore raising a role of autoimmunity in the pathogenesis of T2DM.Thyroid dysfunction is positively correlated with increased cardiovascular risk in women with T2 diabetes

KEYWORDS:

Autoimmune thyroid dysfunction, TSH, Anti TPO, Anti TG, T2 Diabetes, Metabolic syndrome

---

[1]Internal Medicine and Endocrinology, Faculty of Medicine, Cairo University, Cairo-Egypt
[2]Medical Biochemistry, Faculty of Medicine, Cairo University, Cairo-Egypt

SECTION (2): CASE STUDY

Case Study: NAFLD as A Cardiovascular Risk Factor

Nabil Elkafrawy

A 48 years male obese patient complaining of generalized weakness, chronic fatigue, and right hypochondrial dull aching pain. His BMI is 31Kg/m2, WC is 112cm, and the hepatic transaminases are elevated more than three times upper normal level. He had a past history of hypertension and dyslipidemia (hypertriglyceridemia, low HDL-C). No history of alcoholic intake and had a negative viral marker. Ultra-sonography revealed increased echogenicity, Elastography study suggested fatty liver, significant fibrosis and liver biopsy shew steatosis, hepatocyte ballooning and lobular inflammation (components of NASH).

He received treatment for these risk factors, but after 4years he suffered from typical anginal chest pain and accidently discovered diabetes mellitus. He was admitted in CCU for urgent PCI, stented in the left anterior coronary artery and discharged on cardiological and antidiabetic medications.

Definition and causes of NAFLD (1)

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease affects approximately 25% of the adult population. Since NAFLD is frequently associated with further metabolic comorbidities such as obesity, type 2 diabetes mellitus, or dyslipidemia, it is generally considered as the hepatic manifestation of the metabolic syndrome.

NAFLD is also associated with subclinical and clinical cardiovascular disease (CVD) as hypertension, coronary heart disease, cardiomyopathy, and cardiac arrhythmias, which clinically result in increased cardiovascular morbidity and mortality especially those with progressive forms of NAFLD, including non-alcoholic steatohepatitis (NASH) and/or advanced fibrosis, as well as NAFLD patients with concomitant type 2 diabetes.

Differential Diagnosis of NAFLD (2)

Diseases other than the metabolic syndrome can be associated with hepatic fat, and these might enter into the differential diagnosis of fatty liver disease as uncommon causes of NAFLD: (Table)

• Disorders of lipid metabolism as: - Familial combined hyperlipidemia,
- Glycogen storage disease,
- Lipodystrophy.
• Total Parenteral Nutrition. • Wilsons Disease.
• Celiac Disease. • HCV infection.
• Severe surgical weight loss •Starvation.
•Medications: as Methotrexate, Amiodarone, Corticosteroids, etc.…
• Environmental Toxicity.

Clinical Impression

This obese patient had an elevated transaminase, negative viral markers, without history of alcohol intake, ultrasonography revealed increased echogenicity, and the liver biopsy shew steatosis, hepatocyte ballooning and lobular inflammation. So, he could be diagnosed as NASH. Another emerging term could be applied on this patient which is MAFLD (Metabolically Associated Fatty Liver Disease) since he had also some evidence of metabolic dysregulation as hypertension, diabetes dyslipidemia beside the fatty liver.

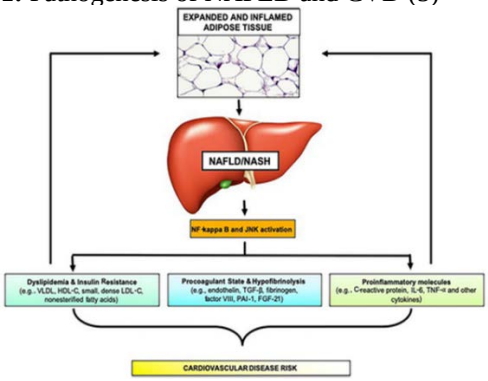
NASH and CVD

A number of studies have shown that NAFLD is a risk factor for CVD and in particular CHD, independent of traditional risk factors (as age, dyslipidemia, hypertension, etc.….) and accounts for at least 40% of total deaths (3).

As NAFLD progresses, expansion and inflammation of intra-abdominal visceral adipose tissue precipitate a proinflammatory cascade through the nuclear factor kappa B (NF-κB) and c-Jun N-terminal kinase (JNK) pathways.

The downstream sequelae are multiple and include systemic/hepatic insulin resistance caused by adipose tissue inflammation with accelerated hepatic steatosis; increased production of inflammatory cytokines by hepatocytes, Kupffer cells, and hepatic stellate cells; synthesis of procoagulant factors with hypo fibrinolysis; and disordered lipid metabolism (4).

Fig 1: Pathogenesis of NAFLD and CVD (5)



CVD Risk Management and Stratification in NAFLD

CVD in NAFLD is associated with traditional and nontraditional CVD risk factors. The Framingham Risk Score (FRS) estimates 10-year rates of CVD events has been validated in NAFLD and may be helpful to risk-stratify individuals and guide treatment of CVD risk factors. A subsequent prospective study in patients with biopsy-proved NAFLD showed that advanced fibrosis on biopsy and higher fibrosis scores were independent predictors of incident CVD. (6)

Of the traditional risk factors, plasma low-density lipoprotein cholesterol (LDL-C) level has shown inconsistent association with CVD in the NAFLD population that may reflect lipid-lowering therapy or advanced liver disease.

Management of our patient with NAFLD (7)

Management of NAFLD must extend beyond liver disease to include CVD risk modification to decrease CVD mortality.

• Healthy diet; in form of High intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, Minimize the intake of trans fats, red meat and processed red meats, refined carbohydrates, and sweetened beverages.

• ≥150 min/week moderate-intensity or ≥75 min/week vigorous-intensity physical activity.

• Stop smoking.

• Nonpharmacological and/or pharmacological therapy with target blood pressure <130/80 mm Hg.

• Statin therapy as the first-line treatment for CVD primary prevention in patients with elevated LDL-C levels ≥190 mg/dL, established diabetes, age 40-75 years, and/or elevated ASCVD score.

• Glycemic control and individualized the target according to the case. Metformin is the first-line therapy, followed by consideration of a SGLT2 inhibitor or a GLP1 receptor agonist with proven CV protection.

Recently, a systematic review and meta-analysis of randomized controlled trials (RCTs) were studied. Besides, three large electronic databases were systematically searched (up to 15 December 2020) to assess the efficacy of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) for treatment of nonalcoholic fatty liver disease (NAFLD) or steatohepatitis (NASH). They concluded that treatment with GLP-1 RAs (mostly liraglutide and semaglutide) is a promising treatment option for NAFLD or NASH that warrants further investigation. (8)

References

1. Sanyal A.J., Brunt E.M., Kleiner D.E., Kowdley K.V., Chalasani N., Lavine J.E., et al. (2011) Endpoints and clinical trial design for nonalcoholic steatohepatitis. Hepatology 54: 344–353
2. Angulo P. (2007) GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmocol Therapeut 25: 883–889.
3. Targher G, Byrne CD, Lonardo A, et al. Non-alcoholic fatty liver disease and risk of incident cardiovascular disease: a meta-analysis. J Hepatol 2016; 65: 589- 600.
4. DeFilippis AP, Blaha MJ, Martin SS, et al. Nonalcoholic fatty liver disease and serum lipoproteins: the Multi-Ethnic Study of Atherosclerosis. Atherosclerosis 2013; 227: 429- 436.
5. Nonalcoholic Fatty Liver Disease and Cardiovascular Disease. Eric M. Przybyszewski M.D.,Giovanni Targher M.D., Michael Roden M.D.et al .CLD Review Article ; 01 February 2021.
6. Henson JB, Simon TG, Kaplan A, et al. Advanced fibrosis is associated with incident cardiovascular disease in patients with non-alcoholic fatty liver disease. Aliment Pharmocol Ther 2020; 51: 728- 736.
7. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019; 140: e563- e595.
8. Alessandro M, Graziano P et al. Glucagon-Like Peptide-1 Receptor Agonists for Treatment of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis: An Updated Meta-Analysis of Randomized Controlled Trials. Metabolites, 2021 Jan 27;11(2):73.

Professor of Internal Medicine and Diabetes, Menoufia University, Egypt

SECTION (3): ARTICLES

Diabetes and COVID 19
Diabetes in patients with COVID 19

Prof. Mohamed Khattab

Co morbidities are common in patients with COVID 19 infection. In a meta-analysis of 8 studies with 46248 patients, it was shown that the most prevalent co morbidity were, hypertension (17 +_7%), Diabetes (8+_6%), cardiovascular disease (5+_4%) and respiratory system diseases (2+_%) (1)

People of any age with type 2 diabetes are at increased risk of severe illness from COVID-19 infection (2). In nationwide analysis in England, it has been shown that type 1 and type 2 diabetes were both independently associated with a significant increased odds of in hospital death with COVID-19. (3)

People with diabetes have an increased risk of infection because of innate immunity defects, increased cytokines, the increased levels of glucose and other metabolites that may be preferred by SAARS-COC-2. Diabetes is a risk factor for the progression and prognosis of COVID-19 (4) The evidence for the link between Diabetes and COVID-19 is not currently fully explained. Several factors especially the impaired immune response, heightened inflammatory response and hyper coagulable state contribute to the disease severity, however, there are many contentious issues about which the evidence is limited such as the role of ACE2 and the theoretical concerns about the effects of different anti-hyperglycemia drugs. (5) Obesity and insulin resistance could mediate the severity of COVID-19 infection. The triglyceride and glucose index which is suggested as a marker of insulin resistance, was closely associated with the severity and morbidity in COVID 19 (6). Moreover, diabetes could be main factor behind accelerated progression of COVID 19 according to a study of Japanese patients (ADA 2021). There hasn't been enough evidence of evidence-based medicine on COVID 19 management in diabetes. Referring to standards of care of type 2 diabetes. IDF refers to follow the recommendations for the SOCK DAY RULES for the patients with diabetes and COVID-19, for better medical care and improved prognosis. Blocd pressure control should follow the guidelines as in non-COVID 19 patients despite the concerns which were raised about the use of RAAS inhibitors. Lipid lowering with statins should continue. Statins has been linked to lower the risk of death from COVID 19 (6)

The relationship between diabetes and COVID 19 appears to be bidirectional. On the one hand, diabetes is associated with increased risk of severe COVID 19. On the other hand, new onset diabetes and severe metabolic complications of existing diabetes including diabetec ketoacidosis and hyperosmolarity for which exceptionally high doses of insulin are warranted have been observed in COVID-19 patients. A potential diabetogenic effect of COVID-19 is hypthesized besides the well-recognized stress response associated with severe illness. (7)

Besides causing severe complications of preexisting diabetes, COVID-19 is suggested to trigger new onset diabetes in healthy people. Evidence from tissue studies and some people with COVID-19 shows that the virus damages the insulin producing cells. (8) Highly ACE2 expression in pancreas may cause pancreatic damage after infection with COVID-19. Potential mild pancreatic injury has been demonstrated in patients with corona virus disease-19 pneumonia (9)

In conclusion:

The variable severity of COVID-19 infection is likely to be multifactorial, Age, sex, severe obesity and diabetes are well established risk factors for increased morbidity and mortality. On the other hand, long term effects of COVID-19 on metabolic health is expected including altered metabolism and development of T2D.

Reference:

1- Yang J et al. Int J Infect Dis.S1201-9712(20)2020
2- CDC Update: July 30, 2020
3- Emma B et al. Lancet Diabetes and endocrinology, August 13, 2020
4- Weina G et al. Diabetes Metabolism Res and Rev March 2020
5- Ritech G et Europ J Clin Nut, 74, 864-870' 2020
6- Ybin w, Cell metabolism. 2020
7- Francesco R et al, New Eng J Med, Aug, 2020
8- Nature 583'16-17 (2020)
9- Fan Wang et al, Gastroentrogy, 159:367-370'2020

Professor of Internal Medicine and Diabetes, Cairo University, Egypt

Leptin: The New & The Old (Minireview)

Samir Naim Assaad, MD, MRCP(UK), FRCP(Edin), FRCP(Lond)

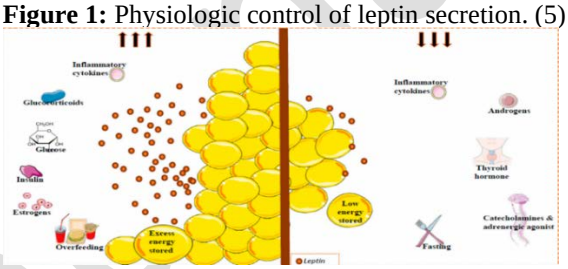
Leptin is produced by white adipose tissue. The main central effects are appetite suppression and increased energy consumption. Leptin synthesis is reduced by weight loss, leading to increased energy uptake and reduction in consumption. Leptin has other beneficial effects related to puberty and immunity. Obesity is associated with increased circulatory leptin levels, which is not able to suppress appetite (leptin resistance). However, this resistance is selective, as hyperleptinemia in obesity is associated with harmful effects (insulin resistance, increased sympathetic activity, hypertension, endothelial dysfunction, inflammation, and platelet activation). Hyperleptinemia has been reported as a risk factor for coronary artery disease.

Leptin therapy is indicated in rare genetic leptin deficiency, lipodystrophy, and anorexia nervosa. Recently, drugs as GLP-1 analogues, oxytocin, uroguanylin (duodenal peptide) and meta-chlorophenylpiperazine (an agonist for both 5-HT2C and 5-HT1B receptors) have been used to reduce leptin resistance.

Leptin is a hormone secreted from white adipose tissue (adipokine). It was discovered in mice by Jeffrey Friedman group in 1994. (1) The nomenclature originated from the Greek word leptós- λεπτός which means thin. Leptin levels are directly proportional to body fat stores. (2) A direct relation is observed between serum leption and BMI. (3) The main physiologic action was considered to decrease appetite and stimulate thermogenesis by inhibiting the orexigenic neurons (neuropeptide Y) and increasing the anorexigenic neurons (cocaine amphetamine related transcript – CART, and proopiomelanocortin) in the hypothalamus. (4)
Unfortunately, serum leptin levels are increased in obesity, with failure to influence appetite control and weight loss. The term leptin resistance was coined, and was postulated to occur at a central level (hypothalamic leptin receptors). (5)
When fat is lost, leptin levels decrease. This stimulates hunger and inhibits satiety, with reduction in resting metabolic rate. This is actually the real and main physiologic effect.

Control of Leptin Secretion:
A Circadian rhythm exits with highest levels in evening and early morning. It is stimulated by glucocortcoids, glucose, insulin, estrogens and overfeeding. It is inhibited by androgens, thyroid hormones, catecholamines and fasting. (5) (Figure 1)
Mean serum leptin is much lower in normal Egyptian men in comparison to women (0.7 ng/ml versus 17.9 ng/ml) (6)

Figure 1: Physiologic control of leptin secretion. (5)



Leptin effects:
Beneficial:

a- Decreased appetite and increase in energy expenditure. (4)
b- Metabolism: (differentiation of preadipocytes to adipocytes, stimulation of lipolysis, conversion of white adipose tissue to brown adipose tissue, control of insulin resistance. In overweight individuals, leptin levels are high, and an increase in preadipocyte number to facilitate the expansion of fat depots could be expected to avoid fat accumulation in other tissues. (2,3,5) Figure 2.
c- Immunity: Immune system competence, stimulation of macrophage adhesion, phagocytosis, and proliferation of T cells (7)
d- Puberty: Leptin has been considered important for puberty induction. A positive correlation was observed between serum leptin and FSH levels during GnRH testing (6)

Harmful (8):

a- Increased sympathetic activity.
b- Hypertension.
c- Endothelial dysfunction.
d- Inflammation.
e- Platelet activation.

Leptin and cardiovascular disease (CVD)

Circulating leptin is considered a risk factor for CVD. (9) A meta-analysis of different prospective studies confirmed hyperleptinemia as an important risk for coronary heart disease (CHD). (10) In a British study, in 550 men with fatal coronary CHD or nonfatal myocardial infarction and in 1,184 controls nested within a prospective setting, a moderate association was observed between serum leptin and CHD that was largely dependent on BMI. (10) A direct correlation was reported between serum leptin and carotid intima media thickness in patients with type 2 diabetes mellitus. (11) Moreover, high circulating levels were reported in patients with dilated cardiomyopathy (12). A comprehensive review of the harmful effects of leptin on the cardiovascular system was published by Katsiki et al. (8) Figure 3.

Figure 2: Metabolic effects of Leptin (5)

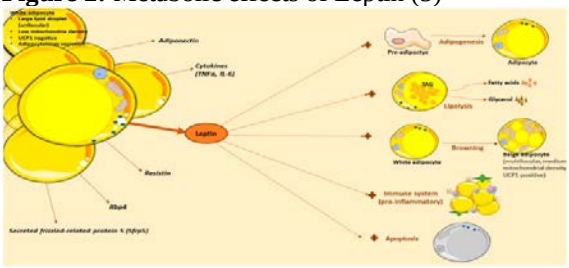
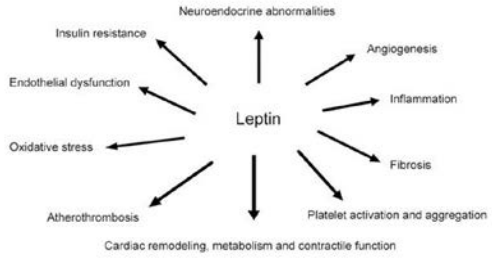


Figure 3: Effects of leptin on the cardiovascular system. (8)



Hyperleptinemia has been involved in the pathogenesis of obesity induced hypertension. In a group of obese Egyptian individuals, serum leptin correlated with mean systemic arterial blood pressure. (3) Selective leptin resistance was observed with preserved agonist effect on the sympathetic nervous system, despite loss of the good metabolic effects of leptin. This can promote for hypertension. (13) Apart from the central effect of leptin to increase vascular tone, a peripheral effect do exist (reduction of nitric oxide, increase in endothelin 1). (14)

Leptin in clinical practice:

The original hope of using leptin to treat obesity actually vanished by the presence of leptin resistance in obese individuals.

Metreleptin (Leptin analog) subcutaneous daily injection has been approved since 2014. (15)

Leptin therapy is useful in rare genetic cases of leptin deficiency. These cases are associated by obesity, insulin resistance/diabetes mellitus (DM), hyperphagia, and high tissue fat/lipotoxicity. (16)

Generalized lipodystrophy is a rare disease characterized by the absence of fat cells, leptin and adiponection secretion. Its clinical features include severe insulin resistance/DM, dyslipidemia (VLDL), fatty liver and pancreatitis. They are corrected with leptin injection. Chronic leptin treatment improves insulin-stimulated hepatic and peripheral glucose metabolism in severely insulin-resistant lipodystrophic patients. Improvement in insulin action leads to reduction in hepatic and muscle triglycerides. Leptin therapy could reverse severe hepatic and muscle insulin resistance and associated hepatic steatosis in patients with lipodystrophy. (17)
Other recent uses of leptin include anorexia nervosa and hypothalamic amenorrhea. (4)

Drugs that increase sensitivity of leptin receptors (agonists) may treat obesity. Chronic oxytocin administration has been advocated as a treatment against impaired leptin signaling or leptin resistance in obesity. (18,19) GLP-1 analogs have been reported to improve leptin resistance. (20) GLP-1 receptor agonist administration may inhibit weight loss-induced increases in soluble leptin receptors thereby preserving free leptin levels and preventing weight regain after weight loss programs or batiatric surgery. (21) Other molecules as uroguanylin (duodenal peptide), meta-chlorophenylpiperazine (an agonist for both 5-HT2C and 5-HT1B receptors), and amylin/ pramlintide decreases have been reported to improve leptin resistance. (22,23) The effects of leptin sensitizers on CVD need to be studied further.

Conclusion:

Obesity is associated with leptin resistance, which makes leptin not useful as a treatment for simple obesity. Selective leptin resistance is associated with harmful cardiovascular consequences. Recent drugs that reduce leptin resistance might be useful tools for the treatment of obesity and cardiovascular protection.

References:

1- Zhang Y, Proenca R, Maffei M, et al. Barone M, Leopold L, Friedman JM. Postional cloning of the mouse obese gene and its human homologue. Nature 1994, 372: 425-32.

2- Liuzzi A, Savia G, Tagliaferri M, Lucantoni R, Berselli ME, Petroni ML, De Medici C, Viberti GC. Serum leptin concentration in moderate and severe obesity: relationship with clinical, anthropemetric and metabolic factors. Int J Obes Relat Metab Disord 1999; 23: 1066-73.

3- Abbassy A.A., El-Din A.G., Cunningham G.R., Atta M.N., Assaad S.N., Rizk M.M., Eid W.E. Study of serum leptin and other hormones in android obesity: relation to hypertension and insulin resistance. The Endocrine Society's 85th Annual Meeting, June 2003, Philadelphia, USA.

4- Seoane-Collazo P, Martínez-Sánchez N , Edward Milbank E , Cristina Contreras C. Incendiary Leptin. Nutrients 2020 Feb 13;12(2):472.

5- Martinez-Sanchez N. There and back again: leptin actions in white adipose tissue. Int J Mol Sci 2020; 21: 6039.

6- Abbassy A.A., Kamel S.S., Assaad S.N., Marzouk S.A., Awad A.B. The relation of leptin and neuropeptide-Y to the hypothalamic pituitary gonadal axis in patients with hypogonadism. The Endocrine Society's 84th Annual Meeting, June 2002, San Francisco, USA.

7- Abella A, Scotece M, Conde J, Pino J, Gonzalez-Gay MA, Gómez-Reino JJ, Mera A, Lago F, Gómez R, Gualillo O. Leptin in the interplay of inflammation, metabolism and immune system disorders. Nature Reviews Rheumatology 2017;13: 100–9.

8- Katsiki N , Dimitri P Mikhailidis DP , Banach M. Leptin, cardiovascular diseases and type 2 diabetes mellitus. Acta Pharmacol Sin 2018 ; 39: 1176-1188.

9- Zeng R, Xu C-H, Xu Y-N, Wang Y-L, Wang M. Association of leptin levels with pathogenetic risk of coronary heart disease and stroke: a meta-analysis. Arq Bras Endocrinol Metabol 2014; 58: 817-23.

10- Sattar N , Wannamethee G, Sarwar N, Chernova J, Lawlor DA, Kelly A, Wallace AM, Danesh J, Whincup PH. Leptin and coronary heart disease: prospective study and systematic review. J Am Coll Cardiol 2009 ; 53: 167-75.

11- Yamazaki Y, Emoto M, Morioka T, Kawano N, Lee E, Urata H, TsuchikurSa S, Motoyama K, Mori K, FukumotoS, Shoji T, Nishizawa Y, Inaba M. Clinical impact of the leptin to soluble leptin receptor ratio on subclinical carotid atherosclerosis in patients with type 2 diabetes. J Atheroscler Thromb 2013; 20: 186-94.

12- Bobbert P, Jenke A, Bobbert T, Kühl U, Rauch U, Lassner D, Scheibenbogen C, Poller W, Schultheiss H-P, Skurk C. High leptin and resistin expression in chronic heart failure: adverse outcome in patients with dilated and inflammatory cardiomyopathy. Eur J Heart Fail 2012; 14: 1265-75.

13- Rahmouni K. Differential Control of the Sympathetic Nervous System by Leptin: Implications for Obesity. Clin Exp Pharmacol Physiol Suppl. 2007 Nov 1; 34 Suppl(s1): S8–S10

14- Rahmouni K, Morgan DA, Morgan GM, Mark AL, Haynes WG. Role of selective leptin resistance in diet-induced obesity hypertension. Diabetes 2005, 54: 2012-18.

15- Chou K, Perry CM. Metreleptin: first global approval. Drugs. 2013 Jun;73(9):989-97.

16- Montague CT, Farooqi IS, Whitehead JP, Soos MA, Rau H, Wareham NJ, Sewter CP, Digby JE, Mohammed SN, Hurst JA, Cheetham CH, Earley AR, Barnett AH, Prins JB, O'Rahilly S. Congenital leptin deficiency is associated with severe early-onset obesity in humans. Nature 1997 Jun 26;387(6636):903-8.

17- Brown RJ, Araujo-Vilar D, Cheung PT,Dunger D, Garg A, Jack M, Mungai L, Oral EA, Patni N, Rother KI, von Schnurbein J, Sorkina E, Stanley T, Vigouroux C, Wabitsch M, Williams R, Yorifuji T. The Diagnosis and Management of Lipodystrophy Syndromes: A Multi-Society Practice Guideline. J Clin Endocrinol Metab 2016 ;101: 4500-11

18- Altirriba J, Poher A-L, Rohner-Jeanrenaud F. Chronic Oxytocin Administration as a Treatment Against Impaired Leptin Signaling or Leptin Resistance in Obesity. Front Endocrinol (Lausanne). 2015 ; 6: 119.

19- Spetter MS, Hallschmid M. Current findings on the role of oxytocin in the regulation of food intake. Physiol Behav 2017 ; 176: 31-9

20- Clemmensen C, Chabenne J, Finan B, Sullivan L, Fischer K, Kuchler D, Sehrer L, Ograjsek T, Hofmann SM, Schriever SC, Pfluger PT, Pinkstaff J, Tschöp MH, Dimarchi R, Müller TD. GLP-1/glucagon coagonism restores leptin responsiveness in obese mice chronically maintained on an obesogenic diet. Diabetes 2014; 63: 1422–1427.

21- Iepsen EW, Lundgren J, Dirksen C, Jensen J-EB, Pedersen O, Hansen T, Madsbad S, Holst JJ, Torekov SS. Treatment with a GLP-1 receptor agonist diminishes the decrease in free plasma leptin during maintenance of weight loss. Int J Obes (Lond) 2015; 39, 834–41.

22- Yan C, Yang Y, Saito K, Xu P, Wang C, Hinton Jr AO, Yan X, Wu Q, Tong Q, Elmquist JK, Fukuda M, Yong Xu Y. Meta-chlorophenylpiperazine enhances leptin

sensitivity in diet-induced obese mice. Br J Pharmacol 2015 ; 172: 3510-21.

23- Folgueira C, Daniel Beiroa D, González-Rellán MJ, Porteiro B, Milbank E, Castelao C, García-Palacios M, Casanueva FF, López M, Diéguez C, Seoane LM, Nogueiras R. Uroguanylin Improves Leptin Responsiveness in Diet-Induced Obese Mice. Nutrients 2019; 11: 752.

Professor of Medicine & Endocrinology, University of Alexandria, Egypt

SECTION (4):
ESDL Previous Events

DiaEgypt 2020

From 14 to 17 October 2020

DGIS Wave 1

From 25 to 26 March 2021 - Hilton Heliopolis - Cairo

Wave 1 رمضان زي السكر

1st of April 2021

DGIS Wave 2

From 12 to 13 August 2021 – Hilton Heliopolis – Cairo

SECTION (5):
ESDL Incoming Events

DiaEgypt 2021

From 6 to 8 October 2021 – Intercontinental City Stars