ABSTRACTS from the 8th Annual World Congress on Insulin Resistance Diabetes & Cardiovascular Disease (WCIRDC)

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ABSTRACTS from the 8th Annual World Congress on Insulin Resistance Diabetes & Cardiovascular Disease (WCIRDC)

AZADIRACHTA INDICA IMPROVES HYPERGLYCEMIA AND PREVENTS HEPATIC GLYCOGENOSIS IN A RAT MODEL OF TYPE 1 DIABETES MELLITUS

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Abstract

We studied the effects of *A. indica* (neem) leaf extract on hepatic histopathology and oxidative status in diabetic rats. Ninety male Wistar rats (8 weeks old) were used. Animals were randomly sorted into five groups of 18 animals each: control; diabetic; diabetic+neem; diabetic+glibenclamide; and neem. Hyperglycemia was induced with streptozotocin (70 mg/kg body weight; i.p). Neem was given orally at 500 mg/kg b.w/d and glibenclamide at 600 µg/kg b.w/d for 50 days (50d). Animals were anaesthetised and sacrificed at 7d, 21d and 50d of treatment. The liver was fixed in Bouin's fluid and stained in PAS; and the levels of lipid peroxides, aqueous hydroperoxide, SOD and GSH were estimated in liver homogenate. Glycemia improved early in neem-treated diabetic rats. However, neem exacerbated the oxidative stress associated with streptozotocin-induced diabetes. At 50d, histopathological study of the liver of diabetic rats showed swollen PAS-positive hepatocytes. Our findings are comparable to diabetic hepatic glycogenosis in human. This pathology was however absent in neem-treated diabetic rats. The major finding in this group was lobular inflammation. Our work thus showed the beneficial effect of *A. indica* in the prevention of glycogenic hepatopathy. However, lobular inflammation and high oxidative stress observed in the liver of diabetic rats treated with *A. indica* indicate association of hepatic lesions with chronic exposure to this herb; and this suggests the need for regular assessment of liver enzymes in diabetic patients on neem therapy.

Key words:

Azadirachta indica, diabetes, liver, glycogenosis, hyperglycemia, oxidative stress

POSTPRANDIAL METABOLIC AND HORMONAL RESPONSES OF OBESE DYSLIPIDEMIC SUBJECTS WITH METABOLIC SYNDROME TO TEST MEALS, RICH IN CARBOHYDRATE, FAT OR PROTEIN

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Background:

The metabolic syndrome (MS) is a cluster of heterogeneous abnormalities, conferring increased risk of cardiovascular diseases. Few postprandial studies have been conducted in MS individuals.

Objectives:

We aimed to study MS subjects with the same abnormalities: abdominal obesity, hypertriglyceridemia and low plasma HDL. We assessed postprandial variations of metabolic parameters related to obesity, dyslipidemia and glucose homeostasis.

Methods:

In this randomized, double-blind, cross-over study, male MS and control subjects consumed, at separate occasions, a high carbohydrate (HC), high fat (HF) or high protein (HP) breakfast meal, providing 30% of each subject's resting energy expenditure.

Results:

Appetite hormones, peptide YY and ghrelin, did not differ between-subject groups. Interleukin-6 was two-fold higher in MS compared with control subjects, consistently with an inflammatory state. Hypertriglyceridemia of MS subjects was aggravated postprandially with the HF and HP meals and was lowest after the HC meal, arguing against increased hepatic VLDL production. HDL-cholesterol of MS subjects remained low postprandially, whereas apolipoprotein (apo) A-II was higher than in control subjects. Unexpectedly, postprandial insulin and glucose responses were higher in MS compared with control subjects, with the HP meal inducing the greater effects.

Conclusions:

The sustained postprandial hypertriglyceridemia of MS subjects after all meals suggests defective catabolism of triglyceride-rich lipoproteins. The greater postprandial increases in plasma insulin and glucose in MS relatively to control subjects indicate decreased insulin sensitivity, not revealed in the fasted state.

CLINICAL PHARMACOGENETICS OF METFORMIN: ROLE OF GENETIC VARIATIONS OF METFORMIN TRANSPORTERS ON THE RENAL CLEARANCE OF METFORMIN

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Abstract

Metformin is an anti-diabetic agent used as first line therapy for Type II Diabetes. The clearance of metformin decreases with decreasing clearance of creatinine, but there is still considerable variation in the clearance of metformin to the clearance of creatinine. Recently, research has focused on the role that metformin transporters play in the absorption, distribution and elimination (primarily renal) of metformin.

Aim:

The aim of the present study was to investigate the relationship between single nucleotide polymorphisms (SNPs) of selected metformin transporters and the clearance of metformin

Methods:
The pharmacokinetics and pharmacogenetics of 104 Type II Diabetics was studied. We examined 62 SNPs of the Organic Cation Transporter 1 (OCT1), Organic Cation Transporter 2 (OCT2), Multi-drug and Toxin Extrusion Protein 1 (MATE1) and Plasma Membrane Monoamine Transporter (PMAT). DNA was extracted from all patients using phenol-chloroform method, amplified by polymerase chain reaction, and analysed using SEQUENOM system. Plasma concentrations of metformin were assayed and metformin clearance calculated using Kinetica population pharmacokinetic analysis software. Statistical analysis was carried out on results using SPSS software.

Results and Discussion:
Creatinine clearance and age account for 40% of inter-individual variation in metformin clearance. The rs644992 and rs9457843 (OCT1 introns) SNP variants were associated with an increased ratio of metformin clearance: creatinine clearance compared to the reference genotype, however there was no significant increase in metformin clearance between the two genotype groups. The rs3822841 (OCT1 intron) and rs2289669 (MATE1 intron) SNP variants were associated with a significant increase in metformin clearance and the ratio of metformin clearance: creatinine clearance. The rs2289669 SNP variant results are in contrast with previous literature on healthy subjects which showed that the variant reduces metformin clearance or has no effect on metformin clearance.

Conclusion:
The rs3822841 (OCT intron) and rs2289669 (MATE 1 intron) SNP variants are strongly assosciated with an increase in metformin clearance and the ratio of metformin clearance: creatinine clearance and may explain inter-individual variation in metformin clearance. Additionally, we hypothesize that the diabetic state induces a change in metformin transport kinetics of the rs2289669 variant.

Keywords:
metformin, transporters, organic cations, genetic variation, renal clearance, diabetes

RELATION OF GAMMA-GLUTAMYLTRANSFERASE LEVELS TO INCIDENCE OF THE METABOLIC SYNDROME

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Abstract
Metabolic syndrome is a cluster of risk factors for cardiovascular disease. Recently, serum gamma-glutamyltransferase(GGT) has been suggested the predictor for development of metabolic syndrome. So we investigated the association between serum GGT levels and incidence of metabolic syndrome in the Korean healthy adults with normal serum GGT for 3 years follow-up period. The study subjects were consisted of 741 individuals who visited Center for Health Promotion in Pusan National University Hospital for a comprehensive medical examination in 2002 and 2005. We measured serum GGT levels, lipid profiles, fasting glucose, blood pressure and their metabolic components. As the quartile of serum GGT increased, 3 years follow-up incidence of metabolic syndrome were increased. Logistic regression analysis adjusting for sex, age, alcohol drinking status showed that odds ratio(95% C.I., P-value) of each GGT quartile was 2.28(0.58~9.01, P=0.240), 1.54(0.36~6.66, P=0.564), 4.56(1.08~19.32, P=0.040). This results showed that serum GGT was closely related with metabolic syndrome. In Korean adults without metabolic syndrome serum GGT levels within normal limit were associated with an increased risk of metabolic syndrome.

Key Words:
GGT; Metabolic syndrome, Insulin Resistance

THE EFFECTS OF INSULIN RESISTANCE ON CYCLE REGULATION AND PREGNANCY RATES FOLLOWING LAPAROSCOPIC OVARIAN ELECTROCAUTERY, IN INFERTILE WOMEN WITH POLYCYSTIC OVARY SYNDROME, RESISTANT TO CLOMIFENE AND METFORMIN

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Objective:
to evaluate the effects of insulin resistance on cycle regulation and pregnancy rates following laparoscopic ovarian electrocautery, in infertile women with PCOS, resistant to clomifene and metformin.

Material:
This is a cohort study. Infertility clinic of Mirza Kuchac Khan Hospital of Tehran University of Medical Science, between 2007 and 2008. Population of study were 54 infertile metformin and clomiphene citrate-resistant women with PCOS. 37 (68.5 %) were non insulin resistant and 17(31.5%) were insulin resistant. Based

on 2 hour plasma insulin after 75 g oral glucose challenge, the patient divided in two groups of insulin resistant (level ≥150 μU/Ml) and non Insulin resistant(level<150 μU/Ml). Both groups underwent LOE and were followed up till 6 months.
Main Outcome Measures: cycle situation and pregnancy rates.

Results:
Of 54 patients 37(68.5%) were non insulin resistant and 17(31.5%) insulin resistant. cycle regulation in insulin resistant patients were less than non insulin resistant after six mounth (OR=0.2 CI: 0.07-0.87).

Pregnancy rate was 32.4% in non insulin resistant, besides laparoscopic ovarian electrocautery, 2 cases with IVF and 1 with IUI achieved pregnancy (Finally 15 cases (40.5%)). Pregnancy rate was 17.6 %(3 cases) in insulin resistant PCOS women.

Conclusion:
Insulin resistance can be an important marker of a poor outcome of infertility treatment. More studies are needed to evaluate the unfavorable influences of insulin resistance and hyperinsulinemia on infertility treatment in PCOS women.

Key Words:
Polycystic ovary syndrome, Insulin resistance, laparoscopic ovarian electrocautery, pregnancy

OBESITY AND GASTROPARESIS IN TYPE 2 DIABETIC PATIENTS WITH NEUROPATHY

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Background:
Associated with neuropathy, symptoms of gastroparesis are common in patients with type 2 diabetes mellitus (T2DM) and include nausea, vomiting, bloating, and early satiety associated with delayed gastric emptying. Gastric motor abnormalities have been reported in obese patients, and obesity is associated with T2DM. An association between obesity and gastroparesis symptoms in diabetic patients with neuropathy has not been investigated.

Methods:
In a cross-sectional survey of gastroparesis prevalence in 380 T2DM patients, 161 were identified as having neuropathy. Gastroparesis symptom prevalence was compared by obesity (BMI≥30kg/m^2). A general linear model of number of symptoms was developed including obesity as a fixed factor.

Results:
Subjects were 66.6±10.years of age, 51% female, diabetes duration 15.6±8.2 years, fasting blood glucose 159±69 mg/dl, HbA1c 8±1.6% and 56.5% obese. Obese subjects reported significantly more early satiety (61.5% vs. 35.2%, p=0.001); fullness (63.7% vs. 40.8%, p=0.004); bloating 70.3% vs. 49.3%, p=0.006) and abdominal distention (71.4 vs. 50.7%, p=0.007) than non-obese subjects. Obese subjects were more likely to have any gastroparesis symptom (RR 2.4, 95% CI 1.01-5.9, p=0.04); moreover, obese subjects reported more gastroparesis symptoms: 4 (0-10) vs. 3 (0-8), p=0.005. In the model of number of gastroparesis symptoms, obesity persisted as a significant, independent predictor even after controlling for age, sex and HbA1c (p=0.03).

Conclusions:
Obesity emerged as a significant, independent predictor of gastroparesis symptoms in patients with T2DM and neuropathy. This finding suggests that mechanisms in addition to neuropathy - perhaps hormones such as ghrelin - play a role in the pathogenesis of gastroparesis in this patient population.

INSULIN RESISTANCE AND METABOLIC SYNDROME IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS EGYPTIAN PATIENTS: CORRELATION WITH DISEASE ACTIVITY AND SERUM LEPTIN

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Abstract
Objective:
To assess the occurrence of insulin resistance and metabolic syndrome and their correlation with disease activity and serum leptin in patients with pediatric SLE.

Methodology:
This study included 30 non-diabetic pediatric SLE patients diagnosed according to ACR revised criteria for SLE and 10 age and sex matched controls. Patients were subjected to full history taking, thorough clinical examination and evaluation of disease activity using SLEDAI. Fasting serum insulin, glucose, leptin, high sensitivity C-reactive protein (HS-CRP) and lipid profile were measured. Insulin resistance (IR) was calculated with the homeostasis model assessment (HOMA-IR). Patients were divided according to International Diabetes Federation (IDF) criteria for metabolic syndrome in children and adolescents into patients with and without metabolic syndrome who were compared regarding disease activity and serum leptin.

Results:
Metabolic syndrome was detected in 9 patients (30%). There was a non-significant difference regarding SLEDAI and HS-CRP

between patients with and without metabolic syndrome. Serum leptin was non-significantly higher among patients with metabolic syndrome than in patients without. There were significantly higher fasting serum insulin and HOMA-IR in patients in comparison to controls. Stepwise multiple regression analysis of factors associated with HOMA-IR revealed that BMI, serum triglycerides and leptin level were the most sensitive independent predictors for IR.

Conclusion:
Pediatric SLE patients are susceptible to insulin resistance and metabolic syndrome regardless of disease activity. Management of metabolic syndrome in these young patients is beneficial to prevent its complications such as type II diabetes and cardiovascular disease.

Key Words:
PEDIATRIC SLE, Insulin Resistance, Metabolic Syndrome, Serum Leptin.

IDENTIFICATION OF NEW TARGET FOR OBESITY AND TYPE II DIABETES TREATMENT BASED ON GENES ASSOCIATED WITH LEAN PHENOTYPE IN HUMAN AND VALIDATION OF THE TARGET BY GENE INACTIVATION IN MICE

Sandrine Braud and Itzik Harosh

Eneteropeptidase Gene Associated With Lean Phenotype in Human and Validation of the Target by Gene Inactivation in Mice.

Background:
Many obesity related genes have been proposed as targets for the treatment of obesity. However, these obesity genes do not provide efficient drug therapy for obesity treatment. It is therefore a challenge to identify crucial gene(s) targets involved in energy metabolism associated with "lean phenotype". In order to identify these genes we have asked the following questions:

- Is there any genetic disease associated with "lean phenotype"?
- Is the phenotype associated with one gene (monogenic)?
- Is the gene target tissue specific?
- Is there any redundancy of the gene target?

Congenital Enteropeptidase deficiency is an extremely rare pathology which answers to all these criteria.

Objective:
Find a new effective target to treat obesity and type II Diabetes.

Methods:
BL6 mice were used to generate KO mice for enteropeptidase, In vivo experiments were done on Swiss mice fed with Diet Induced Obesity, and treated with two doses of OBE lead compound in comparison with control group.

Results:
The KO transgenic mice for enteropeptidase show the same phenotype like in human. The long term treatment (9 weeks) on DIO Swiss mice demonstrates efficacy of OBE lead compound at 10 and 25mg/kg/day with a decrease of around 10% on gain weight. Moreover, in presence of OBE lead compound, triglycerides and proteins absorptions were clearly diminished.

Conclusion:
The proof of concept of enteropeptidase as target for treatment of obesity and type II diabetes was validated with KO mice and OBE lead compound at dose of 10 and 25mg/kg/day in mice.

RAMIPRIL IN TREATMENT OF EXTREMELY HIGH RISK PATIENTS PRESENTED WITH DIASTOLIC DYSFUNCTION AND METABOLIC SYNDROME (RIMS)

Prof. O.M. Drapkina, Prof. V.T. Ivashkin

Purpose:
To investigate ramipril efficiency beyond of its antihypertensive action in the treatment of extremely high risk (SCORE > 15 %) patients with combination of Metabolic Syndrome (MS) and diastolic dysfunction (DD).

Method:
Randomized controlled open-label prospective clinical study has been conducted. Thirty patients with confirmed MS and moderate-to-severe DD were subsequently enrolled in the study and than randomized for conventional therapy including dihydropyridine calcium-channel blockers (CCB) and beta-blockers (BB)±ramipril 10 mg o.d. Patients with direct indications for ACE inhibitors were excluded. We evaluated clinical characteristics, left ventricle (LV) mass, diastolic function (DF) and atrial conduction time using Echo/tissue Doppler imagine fused with ECG, endothelial function (EF) by flow-mediated dilation (FMD), and life quality using SF-36 both before and after 3 month treatment period.

Results:
There were no death and SAE in all patients. Clinically, ramipril use was associated with more significant reduction in dyspnea weakness and chest pain severity. Rampril administration was associated with statistically significant enhancement in DF (E/Em changed from 8.2 to 3.2, $p<0.05$, vs. 8.1 to 7.3, N/S, in control group), decrease of left atrium (LA) volume, heart hypertrophy, acceleration of atrial conduction (from 263 ms to 236 ms, $p<0.05$, vs. 265 to 273 in control group, N/S) and increase in FMD

(+ 14 % vs. + 7 %, p<0.05), see Table. Also we showed statistically significant improvement in life quality accessed by SF-36 in comparison with control group in terms of functional, social activity and global health.

Conclusion:
Rampril on the top of CCB and BB was effective in DF, EF and life quality improvement in extremely high risk patients with IHD, DD and MS. Interestingly, atrial conduction time was accelerated only in ramipril group that might enclose important mechanism of ACE protection against atrial fibrillation.

Parameter	Mean absolute change±SD in ramipril group (n=15)	Mean absolute change±SD in control group (n=15)	P value for difference between ramipril and control groups
LV mass (Deveraux), gr.	–45 ± 10	–15 ± 4	p = 0.03
E/Em	–5 ± 3	–0.8 ± 1	p < 0.01
LA volume, ml	–12 ± 5	–1.2 ± 3	p = 0.04
Atrial conduction time, ms	–27 ± 13	+8 ± 5	p < 0.01
FMD, %	+14 ± 5	+7 ± 1	p = 0.04

SERUM INSULIN LIKE GROWTH FACTOR-1 CONCENTRATIONS IN HEPATITIS C VIRAL INFECTION: A PREDICTOR FOR INSULIN RESISTANCE AND RISK OF DEVELOPING DIABETES IN CHRONIC HEPATITIS C PATIENTS

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Background:
The prospect of the growing worldwide epidemic of Hepatitis C virus (HCV) infection and type 2 diabetes mellitus (DM) certainly merits attention towards their relationship that remains controversial. Insulin-like growth factor-1 (IGF-1) is a liver derived polypeptide, playing an important role in glucose homeostasis. Our aim was to determine the effect of HCV infection on serum IGF-1 concentrations and to explore if IGF-1 is involved in the initial pathogenic mechanisms of diabetes associated with HCV infection.

Methods:
A total of 45 cases; 15 each, chronic HCV, HCV diabetic (HCV/DM) and diabetic patients along with 15 healthy controls were included in the study. HCV RNA was quantified using real-time PCR. Serum IGF-1 levels were measured by ELISA. Homeostasis model assessment of insulin resistance [HOMA-IR], insulin sensitivity [HOMA-S] and β-cell function were determined by previously validated mathematic indexes. Fasting blood glucose, insulin levels and liver biochemical parameters including alanine and aspartate aminotransferases (ALT, AST) were determined, complete Blood picture was also performed.

Results:
Serum IGF-1 levels were significantly lower in chronic HCV, HCV/DM, DM cases than in healthy controls (44.5±8.1; 50.5±5.9 and 144.2±25.9 ng/ml vs. 258.4±36.7 ng/ml, p = 0.001). IGF-1 mean value was significantly higher among HCV RNA negative than positive patients (75.1±29.7 vs. 36.8±5.5, p<0.05). HCV group demonstrated high HOMA-IR and β- cell function levels with positive correlation between HOMA-IR and either β-cell function or fasting insulin levels (p<0.001) also between fasting insulin and β-cell function (p=0.0001), negative correlation between IGF-1 levels and both AST and ALT (p<0.05) and significant positive correlation between HOMA-IR and AST activity (p<0.05). In HCV RNA positive cases, IGF-1 levels were negatively correlated with β-cell function (p<0.01) also with HOMA-IR, however, this correlation didn't reach statistical significance (P=0.074). No correlation was observed between HCV viral load and studied parameters.

Conclusions:
Insulin resistance mediated by IGF-1 but not a lack in insulin secretion might be the primary pathogenic mechanisms implicated in the development of HCV-associated diabetes. Further understanding of IGF-1 signaling may lead to innovative approaches in managing diabetes in HCV patients.

TISSUE LEVELS OF ADIPONECTIN AND LEPTIN IN HUMAN CORONARY ATHEROSCLEROTIC PLAQUES

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Background:
Leptin was originally thought to be an anti-obesity hormone, but it is also a crucial molecule for a number of diverse physiological processes, such as inflammation, immune function and atherosclerosis. Adiponectin has a variety of anti-inflammatory functions against atherosclerosis .There is but little information available

about any link between the levels of adiponectin and leptin in coronary atherosclerotic plaque specimens.

Aim:
We wished to analyses of tissue levels of adiponectin and leptin in the plaques obtained from coronary artery bypass grafting (CABG) and to evaluate whether there is any relationship between these variables and diabetic state.

Patients and Methods:
Thirty-seven coronary atherosclerotic plaque specimens were derived during the elective CABG surgery. Immediately after the procedure, all extracted atherosclerotic plaques were frozen and stored at -80 C until the tissue homogenization.

Coronary artery specimens from thirty seven consecutive patients (28 men and 9 women) at time of CABG procedure and preprocedural blood samples were obtained. Tissue concentrations of adiponectin and leptin in the atherosclerotic plaques were measured.

Diabetes was diagnosed in patients with dietary treatment or antidiabetic medication or current fasting plasma glucose level higher than 7 mmol/l.

Results:
The main finding of the present study that tissue levels of leptin is associated negatively with adiponectin in atherosclerotic plaques. Adiponectin levels were significantly lower in patients with diabetes mellitus than patients without diabetes mellitus. These differences in the variables between the presence and absence of diabetes mellitus remained significant after adjusting for age, gender, BMI, and statin use. Atherosclerotic tissue levels of these substances are also altered in diabetes. The mean tissue levels of leptin is higher in patients with diabetes mellitus than without diabetes mellitus.There was a positive association between leptin and plasma glucose in all patients. Atherosclerotic tissue levels of leptin were significantly higher in patients with diabetes.

The main finding of the present study that tissue levels of leptin is associated negatively with adiponectin. Atherosclerotic tissue levels of these substances are also altered in diabetes.

Table 1. Clinical and Laboratory Characteristics of Study Patients (n = 37)

Characteristics	
Age, years	59.11 ± 10.06
Body mass index, kg/m^2	23.65 ± 3.45
Male, %	75.7
Plasma fasting glucose, mmol/l	6.95 ± 2.81
Tissue concentrations* Adiponectin, µg/ml*	22.97 ± 2.34
Tissue concentrations* Leptin, pg/ml	10503.86 ± 11894.16

Data are mean ± S.D.
*Atherosclerotic tissue levels

Table 2. Comparisons of the Tissue Levels of Parameters between the Patients With (n = 17) and Without (n = 20) Diabetes Mellitus

Parameters	Diabetes mellitus (+)	Diabetes mellitus (-)	*p*
Adiponectin (µg/ml)	21.87 ± 2.05	23.90 ± 2.18	0.006
Leptin (pg/ml)*	3.43 ± 0.07	3.28-3.57	0.006

Conclusions:
Present data provides confirmatory data to prior publications dealing with detection and quantification of various adipocytokines in atherosclerotic plaques. Our results raise a question that diabetic state, in addition to other psychopathological mechanisms, may create a chronic inflammatory situation in atherosclerotic process.

THE ASSOCIATION OF OBESITY WITH ELEVATED ALANINE AMINOTRANSFERASE

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Abstract:
Recently, several obesity related factors have been identified as risk factors for non-alcoholic fatty liver disease(NAFLD) and are also associated with an increase in the risk of hepatocelluar carninoma. However, little is known about the relative importance of obesity marker in the association with NAFLD. We measured ALT in 5,019 Korean adults without a medical history of viral hepatitis, excessive drinking history of alcohol. Anthropometric parameter related obesity and laboratory results were obtained by medical check up program. The average age of increased ALT group was higher than normal ALT group (48.5 vs. 47.4, respectively). All clinical and metabolic variables showed significant differences between subjects with increased ALT group and with normal ALT group (P<0.001). Subjects with increased ALT level also had significantly lower HDL cholesterol (P<0.001). Correlations between increased ALT level and BMI(r=0.216, P<0.001), waist circumference(r=0.197, P<0.001) and triglyceride(r=0.175, P<0.001) was strong positive. These findings suggest that there was positive relationship with increased ALT and obesity related factors.

Key Words:
aminotransferase, obesity, non-alcoholic fatty liver disease, insulin resistance

THE PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN RUSSIAN FEDERATION IN NATIONAL-WIDE DIREG STUDY

O.Drapkina, V.Ivashkin

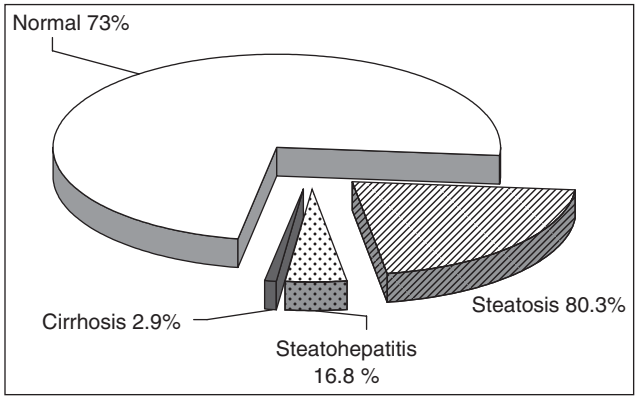
Moscow Medical Academy named by I.M.Sechenov

Non alcogolic fatty liver disease (NAFLD) is obligatory condition of the insulinoresistance in patients with metabolic syndrome.

Aim:
To evaluate the prevalence of non-alcoholic fatty liver disease (NAFLD) in Russian Federation within the national population-based DIGER study.

Methods:
In total of 30 787 primary care patients (56 % females, mean age 47.8±16 yrs) were enrolled into open multicenter national-wide prospective study. Careful clinical examination, serum biochemistry (including ALT, AST, γ-GT, glucose, lipid spectrum and hepatitis screening) and abdominal ultrasound diagnostics with precise liver assessment were performed in 30 754 patients.

Results:
In our study, NAFLD was found in 8215 (27 %) of included patients. Within group with confirmed NAFLD liver steatosis was diagnosed in 80.3 %, steatohepatitis in 16.8 %, and cirrhosis in 2.9 % of patients (see figure). The highest NAFLD prevalence (38 %) was found in patients aged between 50 to 80 years.



Interestingly, only in 3.6 % of NAFLD patients (1.0 % in all population) the diagnosis has been established *before* DIREG-L01903 program initiation, despite regular observations of participants in primary care centers.

Conclusion:
We have shown that NAFLD has very high prevalence (27 %) in Russian population. Direct screening explored that NAFLD prevalence is 27-folds higher comparing with anamnestic data enclosing extremely high rate of underdiagnostics. The attention should be given by primary care physicians for focus diagnosis of this potentially curable disorder.

TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE AND DYSLIPIDEMIA IN PATIENTS WITH METABOLIC SYNDROME USING SIMVASTATIN AND URSODEOXYCHOLIC ACID

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Topics: 6.3 Metabolic/genetic disorders

Introduction:
Nonalcoholic fatty liver disease (NAFLD) is a common condition associated with Metabolic Syndrome (MS). Many patients with NAFLD and MS have hyperlipidemia, their elevated serum aminotransferase levels make physicians wary about prescribing statins. However, the benefits NAFLD and MS patients would derive from statin therapy would most likely outweigh any theoretical risk of liver injury.

Aims & methods:
Ursodeoxycholic acid (UDCA) has been suggested in recent years to be an effective therapy of NAFLD. Combination of UDCA and simvastatin is perspective for the treatment dyslipidemia and NAFLD. Our aim was to assess the efficacy of UDCA and simvastatin in MS patients with NAFLD and dyslipidemia. We examined 40 MS patients (27 men; average age 48±13 years; BMI=33.6 ± 5.2 kg/m^2; waist circumference=113.2 ± 11.1 cm) with clinic, laboratory, ultrasound proven NAFLD and laboratory proven dyslipidemia. Liver biopsy was performed in 18 patients with elevated liver function tests and showed histological findings proven non-alcoholic steatohepatitis (NASH). All patients received UDCA in doses of 15 mg/kg/day and simvastatin 20 mg/day over a period of 6 months.

Results:
In the NASH group the mean serum ASAT levels decreased from 87.2 ± 46.5 to 35.1 ± 15.3 IU/L, serum ALAT levels from 77.9 ± 34.4 to 33.9 ± 16.3 IU/L at the end of the treatment period ($p<0.0003$). After 4 weeks we had no one case of increasing ASAT or ALAT levels on the UDCA and simvastatin therapy. 94.5 % patients (n=17) with NASH reached normal liver function tests. All 40 patients decreased total cholesterol levels from 232.1 ± 48.7 to 170.2 ± 23.3 mg/dl, triglyceride from 263.7 ± 121.6 to 160.3 ± 49.4 mg/dl, LDL from 130.9 ± 49.7 to 82.8 ± 23.7 mg/dl, increased HDL from 40.9 ± 14.1 to 48.2 ± 11.7 mg/dl at the end of the study ($p < 0.000006$).

Conclusion:
A significant improvement in the levels of aminotransferases and lipids levels was obtained with combination of UDCA and simvastatin in NAFLD patients. These results reveal that UDCA and simvastatin may be considered an effective treatment in patients with NASH and MS. Thus, lipid-lowering agents and UDCA should be prescribed for patients with NAFLD unless contraindicated, with careful monitoring of transaminase levels during therapy.

CLINICAL CHARACTERISTIC IN PATIENTS WITH AH AND METABOLIC SYNDROME

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Background:
Hypertension is feature of the Metabolic Syndrome (MS). However, the characteristics of the 24-hour ambulatory blood pressure monitoring (ABPM) in patients with MS are not so well known. Aim of this study was to investigate the clinical characteristics of hypertension in patients with MS by ABPM.

Methods:
We studied 60 subjects with MS according to IDF criteria (36 men, mean age = 48±13 years, BMI = 33±5 kg/m^2, waist circumference (men) = 114±11 cm, (women) = 109±10 cm) and 20 control hypertensive lean subjects. History, physical examination, ECG, ABPM, lipids, fasting glucose and insulin measurements were performed. All patients with MS were insulin resistant (mean HOMA-IR = 5.8±3.6). Hypertension were diagnosed in 88.3 % (n=53) patients with MS according to current guidelines. Non-dipping was defined as a less than 10% fall in systolic ABP from day to night. BP variability was evaluated as the standard deviation day and nighttime ABP.

Results:
The characteristics of hypertension in patients with MS by ABPM were systolodiastolic hypertension daytime, systolic hypertension nighttime, high pulse pressure (PP), high "pressure-time index" (PTI) day and nighttime and prevalence of non-dipping status. Hypertensive patients with MS compared with control group had higher systolic ABP daytime ($p = 0.028$); higher PP ($p = 0.00005$); higher systolic PTI daytime ($p = 0.006$) and nighttime ($p = 0.028$); higher BP variability of systolic, diastolic day and nighttime ABP; impared dipping status with 58% prevalence of non-dippers in hypertensive and normotensive patients with MS ($p < 0.012$). These results demonstrated possible links between insulin resistant and hypertension.

Conclusions:
Our study have shown special characteristics of the ABPM in patients with MS that included high systolic ABP daytime, high PP, high systolic PTI , BP variability and prevalence of non-dippers.

THE DECREASE IN PRODUCTION OF SEX HORMONES AMONG OLDER MEN AND THE DEVELOPMENT OF INSULIN RESISTANCE

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Introduction:
Among people with an age-related decrease in testosterone production, insulin resistance, formed in the process of phylogenesis (Florant G. L. et al., 2004), is used for a compensatory increase in the levels of predecessors of testosterone, cholesterol and glucose (Pechersky A.V. et al., 2006). "Activation by predecessors" is characteristic of many-stage enzymatic processes: an increase in the levels of the preceding substrates stimulates formation of the product of the last stage (Berezov T.T., Korovkin B.F., 2004).

Materials and Methods:
Ten males with partial age-related androgen deficiency and chronic diseases of the tissues of the parodentium were held under study. The patients were prescribed a testosterone preparation in the form of a dermal gel once per day in the morning.

Results:
Expressions of insulin receptors of the mucous membrane of the mouth, as did the data of laser doppler flowmeasuring (under study of microcirculation) increased regularly among the patients studied one month after the beginning of androgen-replacement therapy. The expressions of Ki67 and bcl-2, on the contrary, decreased. Atrophy of the epithelium became less pronounced 1 month after the beginning androgen-replacement therapy in a morphological study of the mucous membrane of the mouth.

Conclusions:
The data received in the study confirm that a reduction in testosterone production in men of older age groups leads to the onset of insulin resistance, increased mitotic activity and a breakdown of microcirculation. The reverse development of the given pathological states takes place under proper androgen-replacement therapy.

RELATIONSHIP BETWEEN FASTING BLOOD GLUCOSE AND BODY MASS INDEX IN THE FEMALE MEDICAL STUDENTS OF CMH LAHORE MEDICAL COLLEGE, AN OBSERVATIONAL STUDY

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CMH Lahore Medical College, Lahore

Object:
To determine the fasting blood glucose levels (FBG) and body mass index (BMI) of the female medical students and to find out any possible relationship between these parameters in the study group.

Methodology:
A cross sectional study was conducted at CMH Lahore medical college from December 2009 to April 2010. A total of 100 medical students participated in this study. A detailed questionnaire was administered to the subjects about personal habits and family history.

Anthropometric parameters and blood pressure were examined by standard methods after taking written consent. Fasting blood glucose levels were examined. Data was assessed by SPSS version 10. Mean Blood sugar fasting levels along with standard deviation were reported. Frequencies of normal, overweight and obese cases were also reported. Analysis included any significant differences in mean FBG levels of the subjects with normal versus obese cases and correlation between BMI and FBG levels was also determined.

Results:
Mean age of our study population was 19.7. Frequency of impaired BMI was found to be 60%. Mean BSF of the subjects having normal BMI was 87.9±4.5 and those with impaired BMI had BSF 94.9±7.4. Mean BSF of the subjects with family history and without family history of diabetes mellitus was 101±6.1and 90.4±6.3 respectively. There was a significant positive correlation observed between BSF levels and BMI.

Conclusion:
Increased BMI may lead to increased level of BSF due to presence of some degree of insulin resistance. Self monitoring of BSF and weight control measures can prevent early onset of diabetes mellitus irrespective of family history of type 2 diabetes mellitus.

Keywords:
Type 2 diabetes mellitus, Body mass index, Fasting blood glucose.

ROLE OF C-PEPTIDE IN PROGRESS OF METABOLIC SYNDROME IN INDIVIDUALS OF SOUTH INDIA WITH TYPE-2 DIABETES MELLITUS

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Abstract
Aim:
The progress of metabolic syndrome continues with the onset of type -2 diabetes mellitus [Type-2DM]. The treatment for such individuals become difficult unless it can be monitored. The aim of this study was to identify the role of C-peptide and correlate it to insulin resistance, BMI, β cell function, insulin sensitivity lipid profile and HbA1c.

Method:
The study design recruited 96 Type-2DM individuals from south India. 58.3males and 41.7 females were selected and fasting blood samples were collected for estimation of fasting C-peptide, FBS, HbA1c, lipid profile and PPBS. Analysis was done on Hitachi 912 & Elecsys 2010 using Roche reagents and standard controls. Antropometry to calculate BMI and β cell function, insulin sensitivity insulin resistance were obtained. Statistical tool ANOVA, P-value, r –value were applied for correlation of c-peptide to HDL-C, LDL-C, triglycerides, HbA1c, β cell function, insulin sensitivity and insulin resistance.

Results:
Highly significant positive correlation emerged in different quintiles of C-peptide to the parameters of metabolic syndrome, BMI and% Beta cell function. Lower HDL was significantly related to the higher C-peptide levels. Similarly TGL and C-peptide was positively significantly Negatively significant correlation occured between c-peptide quintiles and% sensitivity, Thus Insulin resistance showed positive correlation till the 4th quintile. C-peptide and HbA1c had no clear cut relation.

Conclusion:
This study demonstrated that C-peptide is a useful parameter to monitor progress of metabolic syndrome among individuals of type-2DM in south India. When measured with HDL-C it can be used to identify insulin resistance.

Table 7. Quintile distribution C-peptide and Lipid parameters

Quintiles C-peptide	TCL	HDL	LDL	TGL
<2.84	172.95±21.8	47.17±7.93	93.42±25.14	117.11±36.89
2.85-4.19	173.89±35.41	40.52±4.57	106.26±33.21	143.05±44.58
4.20-5.52	158.23±23.94	40.69±5	90.46±22.91	134.68±43.88
5.53-7.05	187.76±44.72	42.7±3.51	111.48±40.38	174.92±66.62
>7.05	171.79±27.13	40.55±4.14	97.89±24.31	196.58±118.89
Significance	0.132	<0.001**	0.197	0.005**

STUDY OF LIPID PROFILE AND MATERNAL ANTHROPOMETRY IN PRE-ECLAMPSIA

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Background:
Pre-eclampsia continues to be a disease of unknown origin and its aetio-pathogenesis is still not very clear, there are no definite and reliable screening methods available for it. Clear understanding of risk factors of pre-eclampsia and its early detection can lead to an increase in long term improvement of the condition.

Tumor necrosis factor (TNF-α) has been shown to cause hypertriglyceridemia[(1)] and level of TNF-α is found to be elevated in preeclampsia women with endothelial dysfunction[(2)]. Disorder of lipid /lipoprotein metabolism, and contributes to endothelial dysfunction in Preeclampsia[(3)].

Aim:
To study the changes in lipid profile in pre-eclamptic pregnancies with special reference to maternal age, parity and severity of hypertension. To study the relationship of pre-eclampsia with body mass index and maternal anthropometry and its pregnancy outcome.

Material and Method:
Forty (40) women with preeclampsia (CASES) and twenty (20) ormotensive pregnant women (CONTROLS), admitted to Department of Gynaecology & bstetrics, JN Medical College and Hospital, in their third trimester, were included in the study. ***Maternal lipids*** i.e Triglyceride (TG), Total Cholesterol (CHOL), High density lipoprotein Cholesterol (HDL-C), Low density lipoprotein Cholesterol (LDL-C), Very low density lipoprotein Cholesterol (VLDL-C) were measured and correlated with Maternal anthropometry, Body mass index (BMI), Midarm circumference (MAC) and pregnancy outcome in the patients of preeclampsia. The values were compared with those of normal pregnant women serving as control.

Results:
Overweight is associated with alterations in lipid concentrations and an activation of inflammatory markers, and both of these metabolic abnormalities are characteristic of pre-eclamptic pregnancies. Physiological pregnancy is associated with a substantial modification of the lipid and lipoprotein metabolism and atherosis is accepted to underlie the pathogenesis of pre-eclampsia(PE).

The observations indicate that serums TG, total cholesterol, LDL, VLDL were increased while HDL was decreased in women with PE, as compared to the women with normal pregnancy. Serum TG, VLDL and LDL also increased with maternal age and parity. Serum TG, VLDL and LDL increased with parity when the maternal age was adjusted. When comparison was done with the severity of hypertension, it was observed that mean serum TG, LDL, VLDL increased as the mean blood pressure of subjects increased, whereas the mean HDL level decreased. Maternal body mass index and Midarm circumference increased with maternal age and parity. While only Midarm circumference was increased with parity when the maternal age was adjusted. The pregnancy outcome in the study showed that weight of infants born to women with preeclampsia was significantly lower than the infants of normal pregnant controls. In this study 35 % of babies born to mothers with preeclampsia were delivered before 37 weeks.

Conclusion:
There is a state of hyperlipidemia in pregnancy that is further aggravated by preeclampsia. Serum TG, VLDL and LDL increased with the maternal age and parity of the subjects. Serum TG, LDL and VLDL increased while serum HDL decreased with increase in the severity of hypertension. There is a significant risk of pre-eclampsia with rise in maternal weight, body mass index the parity and results in increase in risk of preeclampsia. Severity of hypertension is related to increase in maternal weight, body mass index and midarm circumference.Maternal obesity has a detrimental effect on the normal course of pregnancy and it outcome.

Mean birth weight was decreased in infants born to women with preeclampsia.

Keywords:
Midarm circumference(MC) Preeclampsia Maternal lipids Hyperlipidemia fetal outcome

UCP2 SINGLE NUCLEOTIDE POLYMORPHISM -866 G/A IN THE PROMOTER REGION IS ASSOCIATED WITH OBESITY IN A MEXICAN POPULATION

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Background:
Obesity is the most common nutritional disorder in Western society. Approximately 70% of Mexican population has obesity and overweight and Mexico has one of the highest incidences of obesity and overweight worldwide. Uncoupling protein 2 (ucp-2) is a member of the mitochondrial transporter family that regulates uncouples proton entry in the mitochondrial matrix from ATP synthesis. Therefore, we evaluated the association between *ucp-2* -866 G/A polymorphism with obesity in a Mexican population.

Methods:
Sixty obesity patients and 209 control subjects were enrolled after inform consent and examined for the *ucp-2* -866 G/A polymorphism by PCR-RFLP. Clinical and laboratories characteristics were recorded. Data was analyzed by SPSS, version10 software.

Results:
Overall the study population was in Hardy-Weinberg equilibrium. The minor allele A prevalence was significantly higher in obesity patients (0.56) compared with control subjects (0.45). Regression logistic analysis revealed that the A/A genotype significantly associated with obesity in this subjects (OR= 2.5; CI 95%: 1.1-5.8; p=0.034).

Conclusion:
It seems that the *ucp-2* -866 A/A genotype is a risk factor associated with obesity in this Mexican population. Therefore, genetic analysis of single nucleotides polymorphism will help to identify risk groups before they developed chronic diseases.

1. Conflict of Interest:
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INSULIN SENSITIVITY PREDICTS BODY FAT GAIN IN THE FACE OF OVERFEEDING

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High insulin sensitivity is predictive of future weight gain in individuals from populations prone to weight gain. This study seeks to determine if insulin sensitivity is predictive of weight gain in young, healthy, weight stable individuals with imposed energy surplus. Nine lean, physically active subjects (2 women and 7 men, age 26.8 ± 7.0 years, mass 72.0 ± 14.8 kg, BMI 22.6 ± 2.9 $kg.m^{-2}$) recorded their normal (baseline) dietary intake (weighed food record) and physical activity (heart rate) for 1 week. For the following 4 weeks subjects performed identical physical activity and consumed the same diet as during their baseline week plus additional food providing 90 $kJ.(kg\ body\ mass)^{-1}.day^{-1}$ above baseline. Before and after overfeeding, insulin sensitivity was estimated using frequently sampled intravenous glucose tolerance test and body composition was measured using dual x-ray absorptiometry. Subjects body mass increased 3.5 ± 1.8 kg ($p < 0.0019$), body fat % increased from 15.4 ± 4.7 to 16.0 ± 4.7 % ($p < 0.032$) and insulin sensitivity tended to decrease (14.5 ± 5.9 to 9.5 ± 4.1 $min^{-1}.(mU/l)^{-1}$, $p < 0.084$). There was no relationship between insulin sensitivity and body mass. Initial insulin sensitivity was positively related to change in body fat % ($R^2 = 0.80$, $p < 0.002$) and change in insulin sensitivity was negatively related to change in body fat % ($R^2 = 0.60$, $p < 0.02$). Our results indicate that high insulin sensitivity predisposes young lean humans to body fat gain when exposed to excess energy intake.

BENEFICIAL EFFECTS OF *TRIGONELLA FOENUM GRAECUM AND* SODIUM ORTHOVANADATE ON METABOLIC PARAMETERS IN EXPERIMENTAL DIABETES

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Oxidative stress in diabetic tissues is accompanied by high level of free radicals and the simultaneously declined antioxidant enzymes status leading to cell membrane damage. In the present study, the effect of sodium orthovanadate (SOV) and *Trigonella foenum graecum* seed powder administration has been studied on blood glucose and insulin levels, antioxidant enzymes, lipid peroxidation, pyruvate kinase (PK), lactate dehydrogenate (LDH) and distribution of protein kinase C (PKC) in heart, muscle and brain tissues of the alloxan induced diabetic rats and to see whether the treatment with SOV and Trigonella is capable of reversing these effects. Diabetes was induced by administration of alloxan monohydrate (15mg/100gm b.wt.) and rats were treated with 2IU insulin, 0.6mg/ml SOV, 5% *Trigonella* in the diet and a combination of 0.2mg/ml SOV with 5% *Trigonella* separately for 21 days. Blood glucose levels increased markedly in diabetic rats. Rats treated with combined dose of vanadate and *Trigonella* had glucose levels comparable to controls, similar results were obtained with the activities of PK, LDH, antioxidant enzymes and PKC in diabetic rats. Our results showed that lower doses of vanadate (0.2mg/ml) could be used in combination with *Trigonella* to effectively counter diabetic alterations without any toxic side effects. Therefore combined therapy can indeed be considered a better alternative to be explored further as a means of diabetic control.

STUDY OF HYPERINSULINAEMIA INDUCED ACTIVATION OF FARNESYLTRANSFERASE VIA THE RAS-MITOGEN-ACTIVATED PROTEIN KINASE PATHWAY IN ADIPOCYTE

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Clinically the crucial role of insulin is to endorse glucose utilization and also regulate the protein and lipid metabolism. Simultaneously insulin controls mitogenic action like cell growth, cell division, cell migration etc. So a lot of research is being focused on the understanding of insulin action pathway. Recent studies have demonstrated that hyperinsulinaemia stimulates phosphorylation of FTase (Farnesyltransferase) alfa subunit .FTase is a ubiquitous protein as well as a prenyltransferase enzyme that promotes farnesylation of p21 Ras at CAAX motif. Farnesylation of p21 Ras is a requisite step for successive translocation of p21 Ras to the plasma membrane where insulin signaling involves a rapid activation of p21 Ras via stimulation of the guanine nucleotide exchange factor (SOS). SOS promotes an exchange of GTP (active) for GDP (inactive) on

the membrane associated p21 Ras protein. Insulin signaling subsequently activates Raf I, ERK, MAP kinase pathways. Hyperinsulinaemia induced over stimulation of Map kinase, resulting the progression of cancer and atherosclerosis in type 2 diabetic patients where insulin resistance is a common occurrence. We are investigating mitogenic activity of insulin in visceral adipocyte among hyperinsulinaemia affected patients who are treated with metformin (Insulin sensitizer). As an output we noticed that metformin administration improves insulin resistance and prevents the activation of mitogenic factors which are involved in the development of cancer and atherosclerosis .This study helps to understand that the detrimental mitogenic effect of exogenous and endogenous hyperinsulinaemia can be treated by using insulin sensitizing medication.

HYPERINSULINEMIA AND INSULIN RESISTANCE IS ASSOCIATED WITH LOW T3/T4 RATIO IN PRE DIABETIC EUTHYROID PAKISTANI SUBJECTS

Objective:
To investigate the relationship of thyroid hormones in glucose homeostasis in impaired glucose tolerant subjects with normal thyroid functions.

Methods:
Cross sectional analysis was carried out on impaired glucose tolerant (n=130) and normal glucose tolerant subjects (n=130). Thyrotropin (TSH), total triiodothyronine (TT3), total thyroxin (TT4) free T3 (fT3), freeT4 (fT4), and insulin were assessed by enzyme linked immunoassays (ELISA). Fasting plasma glucose (FPG) and HbA1c were measured by glucose oxidase and low pressure cation exchange chromatography. Homeostasis model of assessment (HOMA-IR) was employed to assess the level of insulin resistance, fT3/fT4 ratio was calculated. Anthropometric measurement and habits were recorded.

Results:
Marked hyper insulinemia and insulin resistance was observed in IGT subjects. Serum TT3 levels were significantly low and TSH was elevated in the IGT as compared to normal glucose tolerants (NGT) controls. TT3 had significant and positive correlation with TT4 ($r = 0.700$, $r = 0.577$) in control and IGT respectively ($P<0.01$). Correlation of insulin with TT3, fT3, TSH was significant ($p<0.05$) in IGT subjects. A significant low fT3/ fT4 ratio was observed ($p<0.05$) in IGT subjects ($P<0.01$) as compared to NGT subjects. In multiple regression analysis TSH, TT4 and fT3 contributed significantly to the variance of fasting insulin and insulin resistance in IGT subjects.

Conclusion:
Hyperinsulinemia and insulin resistance is associated with low t3/ t4 ratio in pre diabetic euthyroid pakistani subjects

Key words:
Insulin Resistance, FPG, HbA1c, Thyroid Hormone, fT3/fT4 ratio.

VERY LOW CALORIE DIET-INDUCED EXPRESSION OF CC CHEMOKINE LIGAND – 17 IN SUBCUTANEOUS FAT MAY REPRESENT A NOVEL MECHANISM OF METABOLIC IMPROVEMENTS IN OBESE PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Low-grade inflammation is the key factor linking obesity, type 2 diabetes mellitus and cardiovascular diseases. In this study, we explored the expression profile of genes involved in proinflammatory and adipogenic pathways in subcutaneous adipose tissue (SCAT) and isolated peripheral monocytes (PM) of 12 obese type 2 diabetic patients (T2DM) and 10 healthy lean females (C). The expression analysis of 39 genes in SCAT and PM was performed by RT PCR at baseline and after 2 weeks of very low calorie diet (VLCD).

T2DM group had significantly increased serum concentrations of IL-6, IL-8, TNFα and C-reactive protein and mRNA expression of proinflammatory cytokines (TNFα, IL-6, IL-8, MIF), chemokines (CCL-2, -3, -7, -8, -17, -22, CXCL-10), chemokine receptors (CCR-1, -5) and proatherogenic factors (ICAM-1, VEGF) in both SCAT and PM. mRNA expression of IL-6, leptin, adiponectin was significantly higher in SCAT, while the mRNA expression of chemokine receptors, TNFα, IL-8 and resistin was higher in PM. VLCD significantly decreased body weight, improved glycemia, insulin resistance and lipid profile. VLCD also significantly decreased the expression of chemokine and toll-like receptors (CCR-1,-2,-5, TLR-2,-4) in PM. In SCAT, VLCD reduced mRNA expression of CCL-8, CXCL-10, while CCL-17 mRNA expression markedly increased.

We conclude that T2DM is accompanied by increased mRNA expression of proinflammatory genes in both SCAT and peripheral monocytes. Increased CCL-17 mRNA expression in adipose tissue may play a role in the attenuation of inflammation in adipose tissue and subsequent improvement of metabolic parameters in T2DM patients.

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A PILOT STUDY OF -174 G/C POLYMORPHISM IN THE PROMOTER OF *IL-6* GENE AND TYPE 2 DIABETES MELLITUS IN A MEXICAN MALE POPULATION

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Background:
Mexico has one of the highest incidences of T2DM, obesity and overweight worldwide. Several prospective studies have found an association between elevated levels of interleukin 6 (IL-6) and T2DM. IL-6 is a pleiotropic cytokine, which has been linked with the phosphorylation of insulin receptor substrate 1 (IRS-1); a key molecule for the translocation of glucose transporter protein 4. Therefore we assessed the *il-6* -174 G/C polymorphism distribution in both Mexican parental unrelated individuals with T2DM and control subjects.

Methods:
121 T2DM patients (78 males and 43 females) and 212 healthy control (86 males and 126 females) subjects of both gender, were enrolled after inform consent. Anthropometrics' characteristics were recorded. A blood sample was taken for DNA extraction and the *il-6* -174 G/C polymorphism was determinate by PCR-RFLP. Data was analyzed by SPSS, version10 software.

Results:
Of the 121 patients 39% were overweight (≥25 to <30kg/m^2), 21% had central obesity (waist >90cm for male and >80cm for women). The C allele distribution in the whole population was similar, 0.08 for T2DM patients and 0.11 for control subjects. After adjustment for age, body mass index, glucose, total cholesterol and tryglicerides, GG genotype was only associated with diabetes in males (OR= 0.34; CI 95%: 0.13-0.87).

Conclusion:
Overall our results suggest that *il-6* -174 G/G genotype is an independent protector factor associate with T2DM for Mexican males, probability reducing diabetes susceptibility in these subjects.

1. Conflict of Interest:
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HIGH INSULIN AND C-PEPTIDE: CLOSE ASSOCIATIONS WITH HYPERTRIGLYCERIDEMIA AND HYPOALPHALIPOPROTEINEMIA

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Background:
We hypothesized that concurrent fasting high serum insulin (I) (>29.1 IU/ml) and C-peptide (CP) (>5), with normal fasting blood glucose <126 mg/dl were associated with hypertriglyceridemia (HTG) and low HDL cholesterol (HDLC) in patients referred for diagnosis and treatment of hyperlipidemia.

Methods:
In the sequential order of their referral, we studied 73 patients with high I and CP, 2004 with normal I (<=29.1) and CP (<=5), all with glucose < 126 mg/dl. TG was classified as per the NCEP (<150 mg/dl normal, 150-200 borderline high, 200-500 high, >=500 very high), as was HDLC (<40 mg/dl low, >60 high). Categorized by high I-high CP and normal I-normal CP, TG and HDLC distributions are shown in the table.

Results:
Concurrent high I and CP with normal glucose was associated with a skewing of TG to high and very high levels and with skewing of HDLC to low and very low levels. In the total cohort of 2297 patients (including 220 patients with glucose >=126 mg/dl, 26 high I-high CP, 194 normal I-normal CP), the correlation of I with TG was r= 0.39 (p<.0001), and I with HDLC was r= –0.34 (p<.0001). The correlation of CP with TG was r= 0.44 (p<.0001), and with HDLC was r= –0.36 (p<.0001). The correlation of HOMA insulin resistance with TG was r= 0.42 (p<.0001), and with HDLC was r= –0.33 (p<.0001).

Conclusion:
The close associations of high I and CP with TG and HDLC in patients with glucose < 126 mg/dl speculatively suggests that reduction of insulin resistance with metformin and/or PPAR-beta agonists may be therapeutically useful and synergistic with fibric acid therapy in normalizing TG and HDLC in patients with high TG and low HDLC.

TG (mg/dl)	n	median	<150	150-200	200-500	500-1000	>or=1000	X2	p
High I & CP	73	271	15%	21%	44%	16%	4%	25.7	<.0001
Normal I & CP	2004	147	51%	14%	27%	6%	2%		
HDLC (mg/dl)	n	median	<30	30-40	40-50	50-60	>60	X2	p
High I & CP	73	37	27%	36%	30%	7%	0%	50.9	<.0001
Normal I & CP	2004	47	9%	23%	28%	20%	20%		

ASSOCIATION OF INSULIN RESISTANCE WITH LIPID PROFILE IN IMPAIRED GLUCOSE TOLERANT PAKISTANI SUBJECTS

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Abstract

The objective of the present study was to determine the relationship between lipid profile and insulin resistance in impaired glucose tolerant subjects. A total number of 508 subjects (male n = 228, female n = 280), age between 38-60 years, were included in the study. All subjects underwent a 75 g oral glucose tolerance test (OGTT) for the diagnosis of IGT. Insulin was assessed by Immunoenzymometric assay (ELISA). Homeostasis model assessment (HOMA-IR) was employed. Total cholesterol, HDL, LDL, VLDL and triglycerides were assessed using an enzymatic colorimetric kit processed in automatic chemistry analyzer. Fasting plasma glucose and HbA1c were measured by glucose oxidase and low pressure cation exchange chromatography. Anthropometric measurements including BMI, WHR, Waist circumference, family history and habits were recorded. Analysis was performed by using software SPSS Version 13 (Chicago, IL, U.S.A.).

A substantial number of IGT was found based on OGTT (48%) and fasting glucose level detected 52% of the subjects. IGT subjects were insulin resistant and hyperinsulinemic with significant lipid abnormalities. Gender differences were significant ($p<0.05$). The correlation between HOMA IR and BMI was $r= 0.89$, $p<0.0001$. Serum fasting insulin level was correlated with triglycerides and LDL cholesterol ($r=0.95$, $p<0.0001$, $r=0.37$, $p<0.01$) respectively. Both measures were strongly correlated with HOMA-IR and two hours post challenge glucose level ($r=0.97$, $p<0.0001$, $r=0.39$, $p<0.001$) respectively.

Conclusion:

The strongest correlation was found between IR and triglyceride levels ($p<0.0001$). IGT forms an important target group for interventions and therapeutic targets.

Key words:

BMI, Serum fasting insulin, triglycerides, HDL, LDL, IR.

ASSOCIATION OF CIRCULATING LEPTIN AND METABOLIC RISK FACTORS IN NORTH INDIAN ADULT WOMEN

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Abstract

Leptin plays an important role in the regulation of body weight and it operates by inhibiting food intake and stimulating energy expenditure. The purpose of the present study was to investigate the association of serum leptin level and metabolic risk factors (MRF) in North Indian adult women. In a case-control study, out of 390 women, 186 women with metabolic syndrome (MetS) according to the criteria of National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP) guidelines and 204 healthy control women without metabolic syndrome (wMetS), ages between 20-40 years old were recruited for the study. Circulating leptin levels was determined by sandwich ELISA method, Insulin resistance by the homeostasis model assessment (HOMA) index and lipid profile by enzymatic method. Circulating leptin (13.38 ± 9.00 vs. 8.16 ± 6.31 ng/ml, $p<0.01$), HOMA-IR 2.68 ± 2.05 vs. 1.72 ± 1.20, $p<0.01$), lipid profile ($p<0.01$) and other MRF viz. WC, WHR, BMI, FPI were found significant among MetS women and wMetS. According to NCEP ATP III criteria for MetS women, MRF were significantly high ($p <0.01$) in MetS compared to wMetS women. Serum leptin level was positively correlated with HOMA-IR ($p=0.000$) and other metabolic risk factors including WC, WHR, BMI, SBP & DBP, TC, TG, TC/HDL-C ratio, FPG and FPI except with HDL-C ($p=0.024$) in North Indian adult women. The study concluded that circulating leptin is significantly associated with hyperlipedemia, insulin resistance and with other metabolic risk factors in North Indian adult women.

Key Words:

Leptin; Insulin resistance; lipid profile; metabolic risk factors

SERUM RESISTIN LEVEL VS METABOLIC SYNDROME: EVIDENCE BASED EPIDEMIOLOGICAL STUDY IN HUMAN MALE VOLUNTEERS

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Abstract

Resistin, a member of class of cysteine-rich proteins, has reported to be associated with obesity induced insulin resistance and metabolic syndrome. However, the physiological functionality of

resistin in human beings is still poorly understood and remains to be established clinically. Thus, the present investigations were carried out to study the association, if any, between serum resistin levels and metabolic syndrome in human male volunteers residing in northern part of India. Of the total 386 volunteers enrolled in the study following the criteria of National Cholesterol Education Program-Adult Treatment Panel III- 2001, 192 aged 33.40±4.67 years were the diagnosed cases of metabolic syndrome, while rest 194 aged 31.07±6.08 years were designated as control. In cross sectional study, a positive correlation between serum levels of resistin Vs levels of serum insulin, glucose, lipids profile, blood pressure, waist circumference, waist/hip ratio could be established. Serum resistin levels (12.49±4.73ng/ml n=192) were found to be significantly ($p<0.001$) higher in volunteers having metabolic syndrome, when compared with control volunteers without metabolic syndrome (6.98±1.98ng/ml; n=194). Our data indicates the significant association between serum resistin levels and metabolic syndrome and could be an early non-invasive marker with high predictive values; however, further studies to identify the resistin specific cellular receptor are needed.

Key Words:
Resistin; Metabolic Syndrome; Insulin Resistance

ASSOCIATION OF TNF-A PROMOTER GENE G-308A POLYMORPHISM WITH METABOLIC SYNDROME, INSULIN RESISTANCE, SERUM TNF-A AND LEPTIN LEVELS IN INDIAN ADULT WOMEN

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Abstract

Background:
Tumor necrosis factor alpha is a multifunctional pro-inflammatory cytokine involved in the pathogenesis of metabolic syndrome, Insulin resistance, and obesity. Aim of this study is to investigate in a North Indian female population the impact of the G-308A TNF-α variant on various components of the metabolic syndrome, Insulin Resistance, serum TNF-α and Leptin levels.

Methods:
The G- 308A TNF-α polymorphism has been studied in 269 females with Metabolic Syndrome (NCEP ATP III criteria) (Age 31.91 ± 6.05) and 272 healthy females without Metabolic Syndrome (Age 30.96 ± 7.01). The G-308A variant was detected by PCR amplification and Nco-1 digestion.

Results:
Homozygous mutant genotype (AA) ($p=<0.001$: OR=3.24: 95% CI= 2.15-4.89) and mutant allele (A) ($p=<0.001$: OR=3.04: 95% CI= 2.08-4.43) of TNF-α was significantly less frequently observed in the control population as compared to study group. Furthermore, on dividing the subjects into two groups according to the absence (TNF-1 allele) or presence of the mutant A (TNF-2) allele, significant results were obtained in most of the metabolic risk factors, TNF-α and Leptin levels.

Conclusions:
The G-308A polymorphism of the TNF-α gene is likely to be associated with visceral obesity and metabolic syndrome independent of Insulin resistance and hyperglycemia.

Keywords:
TNF-alpha; Leptin; Metabolic Syndrome; PCR; HOMA Index

LEPTIN TO ADIPONECTIN RATIO AS A POTENTIAL BIOMARKER FOR THE METABOLIC SYNDROME

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Background and purpose:
Recent studies have been reported that adiponectin and letin are associated with the metabolic syndrome. The evaluation of the leptin/adiponectin ratio has been suggested as an atherosclerotic index. The objective of this study was to compare the strength of between metabolic syndrome and adiponectin, leptin and leptin/adiponectin ratio.

Methods:
The study population consisted of 9,995 subjects, who participated in the Korean Metabolic Syndrome Research Initiative and had routine health examinations at the Health Promotion Center at University Hospitals from 2006 to 2007. Among the study population, 3,487 individuals were randomly selected for measurement of serum leptin and adiponectin. Each participant was interviewed using a structured questionnaire. Adipokines were divided into quartiles and metabolic syndrome was defined by NCEP ATP III. The logistic regression model was performed to establish the association between adipokines and metabolic syndrome.

Results:
The adiponectin, HMW adiponectin, and leptin were correlated with the metabolic syndrome components, and leptin of these adipokines

was highly correlated with waist, body mass index, and HOMA. Leptin/adiponectin ratio in the highest quartile were associated with 5-fold increased odds of prevalent metabolic syndrome independent of age, smoking status, exercise, LDL cholesterol, and body mass index as compared with the lowest quartile. There was a linear increase in the leptin/adiponectin ratio with increasing numbers of the metabolic syndrome components. Leptin/adiponectin ratio had the highest area under the curve (AUC) for metabolic syndrome.

Conclusion:
This study demonstrated that leptin/adiponectin ratio had a more significant association with metabolic syndrome than other adipokines.

ASSOCIATION OF ADIPONECTIN 45 T/G AND 276 G/T GENE POLYMORPHISM WITH INSULIN RESISTANCE AND THEIR CIRCULATING ADIPONECTIN LEVEL IN SUBJECTS WITH METABOLIC SYNDROME

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Abstract
Background:
Adiponectin has been shown to be an insulin-sensitizing hormone, is an adipose tissue-specific protein of 247 amino acids and are negatively associated with metabolic syndrome.

Aim:
The study to investigate the association of adiponectin gene polymorphism (45 T/G & 276 G/T) with metabolic syndrome, Insulin resistance and their adiponectin level in north Indian adult women.

Methods:
The Adiponectin T-45G & G-276T polymorphism has been studied in 269 females with Metabolic Syndrome (MetS) and in 272 healthy females without Metabolic Syndrome (wMetS) according to NCEP ATP III criteria, 2001. Circulating Adiponectin level was determined by sandwich ELISA method and Insulin resistance by the homeostasis model assessment (HOMA) index. The polymorphism of Adiponectin 45 T/G and 276 G/T gene were analyzed by PCR-RFLP method.

Results:
Significant difference was found for circulating adiponectin level (20.21±10.85 vs. 29.56±13.46) and for metabolic risk factors among MetS and wMetS females. Mutant genotype (GG) (TT vs TG+GG) (p=0.0169: OR=1.55: 95% CI= 1.09-2.19) and allele (G) (p=0.0080: OR=1.49: 95% CI= 1.12-1.99) of the T-45G gene & mutant allele (T) (p=0.0278: OR=1.36: 95% CI= 1.04-1.77) of the G-276T polymorphism were significantly less frequently observed in the wMetS population as compared to MetS women.

Conclusions:
The results of the present study concluded that the mutation of the Adiponectin 45 T/G & 276 G/T gene might play a important role in obesity associated metabolic syndrome in the north Indian females due to mutation of the adiponectin gene is associated with decreased adiposity which is protective one for metabolic syndrome.

Keywords:
Adiponectin gene, level, Insulin resistance, metabolic syndrome

IDENTIFICATION OF CARDIOMETABOLIC RISK IN MEDICAL STUDENTS

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Objective:
To determine the prevalence of cardio metabolic (CMR) risk factors in medical students of a government medical college of Karachi.

Subject and methods:
We conducted a cross-sectional study on students of Dow Medical College, Karachi, Pakistan. Measurements were taken for assessing blood pressure, height and weight. A pretested self-administered questionnaire was used to collect other data. Blood pressure and height/weight (for calculating BMI) was noted by trained observers and physical activity level was determined through the WHO Global Physical Activity Questionnaire (GPAQ). SPSS 15.0 was used for statistical analysis. Cardio metabolic risk was determined on the basis of presence of elevated blood pressure, personal or family history of cardiovascular disease (CVD), overweight, smoking, alcohol consumption, low physical activity level, incorrect self-assessment (underestimation) of weight, low knowledge about cardio metabolic risk factors and lack of interest in consuming cardio protective diet. An arbitrary scale was made for assessing cardio metabolic risk on the basis of above mentioned risk factors. Score obtained by each student on CMR scale was calculated.

Results:
Non-probability purposive sampling was used and a total of 132 medical students were included in the study of which 57 (43.2%) and 75 (56.8%) were male and female respectively with overall

mean age of 20.85 ± 1.21 years. Males had significantly higher mean cardio metabolic risk score as compared to females. This was largely due to difference in presence of elevated blood pressure (43.9% males vs. 14.7% females, p = 0.000), lack of interest in consuming cardio protective diet (26.3%m vs. 2.7%f, p = 0.000) and underestimation of weight (14%m vs. 0%f, p + 0.01). Family history of CVD (57%) and low physical activity level (38%) were the most common cardio metabolic risk factors.

Conclusion:
Presence of family history in large number of students, high rates of elevated blood pressure and lack of knowledge and interest in modifying behavior indicate urgent need for motivating students for taking interest in their own cardio metabolic heath. The situation reflects potential of future physicians for encouraging their patients to modify their health related behavior.

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INCIDENCE OF HYPERINSULINEMIA IN COLLEGE FRESHMEN STUDENTS

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College years are commonly associated with weight gain, improper diet, lack of physical activity and increased stress, all placing one at risk for the development of insulin resistance (IR) and hyperinsulinemia. The primary goal was to establish a baseline measurement of fasting insulin, and other variables known to influence insulin sensitivity in a group of college freshmen. Blood was drawn from 22 students after a twelve-hour overnight fast and analyzed for insulin and glucose. BMI was determined and subjects completed a short questionnaire determining age, ethnicity, family history of diabetes, and patterns of physical activity, diet, and stress. BMI values classified one third of the subjects as overweight. Eight of 22 subjects (6 women and 2 men) were defined as hyperinsulinemic. A Risk Score was developed to summarize each subjects data, and all subjects classified as low risk had insulin values < 14 μU/mL. There were significant differences in fasting insulin when subjects were grouped by BMI ($p<0.01$), genetic predisposition ($p<0.007$), and RISK Score ($p<0.0000067$). This is the first study in which fasting insulin, and the incidence of hyperinsulinemia has been reported in a mixed group of college freshmen. Data allows tracking of students to determine if anticipated changes in lifestyle during college are accompanied by changes in circulating insulin levels. Identifying students who are experiencing hyperinsulinemia, and therefore are at greater risk for chronic health issues, should prove invaluable as patterns established in college will likely continue as students leave college and live adult lives.

PYCNOGENOL® ATTENUATES HYPERLIPIDEMIA, RENAL FUNCTION MARKERS AND ANTIOXIDANT RESPONSES IN PANCREAS TISSUE OF TYPE 2 DIABETES ANIMAL MODEL

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Abstract
Diabetes mellitus is a pathologic condition, resulting in severe metabolic imbalances and non-physiologic changes in many tissues more particularly in pancreas, where oxidative stress plays an important role in the etiology. Pycnogenol® (PYC), a patented combination of bioflavonoids extracted from French maritime pine (Pinus maritima) bark, is used extensively as a dietary food supplement because of its high antioxidant capacity. The present study was design to evaluate the beneficial effect PYC on hyperglycemia, renal damage, lipid profile and oxidative damage in the pancreas of normal and diabetic rats. Diabetes was induced by feeding rats with high-fat diet (HFD; 40%) for two weeks followed by streptozotocin (STZ; 40 mg/kg body weight; intraperitoneally (IP)). Four days after STZ injection rats were supplemented with PYC (10 mg/kg body weight) for four weeks. At the end of the experiment, blood was drawn and rats were then sacrificed and their pancreas was dissected for biochemical and histopathological assays. The level of fasting blood glucose, glycated hemoglobin, total cholesterol, triglycerides, low density lipoprotein-cholesterol and very low density lipoprotein-cholesterol significantly increased while high density lipoprotein cholesterol and hepatic glycogen decreased in the HFD/STZ group. PYC treatment significantly augmented ($P < 0.05$) these effects in the HFD/STZ + PYC group. The HFD/STZ group showed elevated renal injury markers in serum, including blood urea nitrogen, serum creatinine and alkaline phosphatase, which were decreased significantly ($P < 0.05$) by PYC treatment. Moreover, treatment with PYC significantly ($P < 0.05$) ameliorated thiobarbituric reactive substances, malonaldehyde and protein carbonyl, and glutathione, glutathione-s-transferase and catalase in the pancreas of the HFD/STZ group. The study suggests that PYC is effective in reducing hyperglycemia, hyperlipidemia and oxidative stress related to the risk of diabetes. Thus, it may have a therapeutic value for the treatment of Type 2 diabetes.

Keywords:
Pycnogenol; Type 2 diabetes; Oxidative stress; Streptozotocin

METABOLIC ABNORMALITIES AMONG MEXICAN CHILDREN AND ADOLESCENTS WITH OVERWEIGHT AND OBESITY

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Background and aims:
Prevalence of overweight (OW) and obesity in children 2-18 years old in Mexico is Half of the obese children become obese adults. Obesity dysregulates metabolic processes including action of insulin on glucose and lipid metabolism, and blood pressure. Insulin resistance (IR) is a key factor influencing and driving metabolic alteration. The aim of the present study was to determine the frequency of metabolic abnormalities (hyperglycemia, dyslipidemia, insulin resistance), and high blood pressure among Mexican children and adolescents with overweight and obesity.

Methods:
A cross sectional study was performed in 120 subjects (60 scholars and 60 adolescents), ages of 8.2±1.3 and 13.6±1.4 years, respectively. Fasting serum triglycerides, cholesterol, HDL-c, glucose and insulin levels were determined. Overweight and obesity were established as BMI≥ percentile 85 and BMI≥ percentile 95; respectively. High blood pressure (≥ percentile 90). Clinical and anthropometric parameters were performed. Chi square and t test were used for data analysis.

Results:
The most frequent metabolic alterations were elevated concentration of triglycerides (60%), hypercholesterolemia (61%), low HDL (19%) and hyperglycemia (6%). High blood pressure was found in scholars (25%) and adolescents (31%). Elevated waist circumference (CC≥ percentile 85) was observed in 80% of the sample and it was associated with high insulin levels (r=0.274, p 0.002).

Conclusions:
The same risk factors associated with cardiovascular morbidity and mortality in adults were found in obese children and adolescents in the present study. Infantile obesity is a risk factor of hyperinsulinemia and subsequent metabolic alterations underlying cardiovascular disease in obese children.

INCIDENCE OF RETINOPATHY DETECTED BY FUNDOSCOPY AMONG NEWLY DIAGNOSED TYPE 2 DIABETIC PATIENTS VISITING AMIN HAYAT MEMORIAL HOSPITAL LAHORE- PAKISTAN

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The prevalence of diabetes in Pakistan is increasing at alarming rate.This cross-sectional study was conducted on 200 consecutive newly diagnosed diabetic patients to asses the incidence of diabetic retinopathy and to evaluate its relationship with potential risk factors of insulin resistance on their first visit to Amin Hayat Memorial Hospital Lahore. Diabetic patients with age group 40-60 (both sexes) were included in the study. Four groups based on fundoscopic examination were made as N (normal), BDR (background retinopathy), Pre-Proliferative and Proliferative. Different demographic parameters as age, gender, BMI, B.P, personal history, socioeconomic status were calculated. The biochemical parameters included FBG, RBG, HbA1c, lipid profile and insulin.

Among the diabetic subjects 33% (n=60) were retinopathic. Out of which 29% (n=19) were male and 70% (n=46) were female. The FBG (mg/dl), RBG (mg/dl), HDL (mg/dl), both systolic and diastolic blood pressure (mm of Hg), insulin (ulU/L) and cholesterol level were significantly higher ($p< 0.05$) in proliferative group of diabetic retinopathy while triglyceride level(mg/dl), HbA1c(%), and LDL(mg/dl) were non significantly higher ($p> 0.05$) in diabetic retinopathy groups.

High prevalence of diabetic nephropathy was observed. This underscores the importance of detailed ophthalmic examination of all diabetic patients at the time of diagnosis.

Keywords:
Fundoscopy, retinopathy,proliferative, BDR.

NON-ALCOHOLIC FATTY LIVER DISEASE IS AN EARLY PREDICATOR OF SELECTIVE INSULIN RESISTANCE AND A COMPLIMENTARY RESPONSE OF IMPAIRED GLUCOSE METABOLISM

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Objective:
To analyze the correlation of Non-alcoholic Fatty Liver Disease (NAFLD) with insulin resistance and glucose metabolism.

Methods:
Clinical manifestation and laboratory results were collected in nineteen patients with NAFLD and 17 controls without NAFLD. The patients in both groups took 75g oral glucose tolerance test and the serum glucose level, C peptides, insulin were measured and HOMA index were calculated at different time point. The

quantification of liver fat was done by H^1MRS and the fat content over 5 % were recruited to the NAFLD group.

Results:
Serum ALT, TG and glucose level, serum insulin were significantly high in NAFLD group and HDL level were significantly lower than that of control group (1.14 vs. 1.69). The insulin secretion are normal or higher in NAFLD patients but it decreased significantly in NAFLD patients with IGT or diabetes with increased r-GT, which mean the β-cell dysfunction in NAFLD patients with diabetes.

Conclusions:
The insulin resistance was closely related to NAFLD and represented by high secretion of insulin at early beginning. Hyperinsulinism is the major manifestation of fat accumulation in the liver. The NAFLD patients will develop into diabetes with the failure of β cell secretion and impaired glucose metabolism. It is very important to manage NAFLD earlier to prevent the impaired of glucose metabolism and β cell failure. We assume the fat accumulation and hyperinsulinism is a complimentary process and early predictor of dysfunction of glucose metabolism**.**

Key words:
Non-alcoholic fatty liver disease; Insulin resistance; Glucose metabolism

ALTERED GENE EXPRESSION IN ADIPOSE TISSUE OF THE INTRAUTERINE GROWTH-RESTRICTED RAT OFFSPRING

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Background:
Nutrition during fetal and early postnatal development can have permanent effects on physiology resulting in an increased risk for disease in later life. The aim of this study was to explore changes in gene expression related to maternal energy restriction during pregnancy in adult male rat offspring.

Methods:
The intrauterine growth-restricted rat offspring (IUGR) rats exposed to either prenatal, postnatal, or pre- and postnatal nutrient restriction were compared with age-matched controls. Genes involved in glucose transport, fat metabolism and ageing were determined in adipose tissue by semiquantitative RT-PCR.

Results:
Maternal undernutrition induced visceral adiposity in the offspring. Results show extensive alterations in mRNA expression of genes involved in glucose transport (glut4); lipogenesis (visfatin, resistin, leptin, adiponutrin, fatty acid synthase, fatty acyl transport protein 1, Acetyl-CoA carboxylase-α, stearoyl-Coenzyme A desaturase 1); inflammation (TNF – α); ageing(Sirtuin 2 and FOXO1) and also some nuclear receptors (PPAR γ, SREBP1and SREBP2). The altered expression of above genes might have an important role in the development of obesity and insulin resistance in the IUGR offspring.

Conclusion:
Thus visceral adiposity in this rat model is marked by dynamic changes in the transcriptional profile of visceral adipose tissue. Our data provide new insights into the molecular mechanisms that underlie the developmental programming of visceral adiposity.

STUDIES ON PHYTOCHEMICALS CHARACTERISTICS, NUTRIENT CONTENTS, AND HYPOGLYCEMIC ACTIVITIES OF MOMORDICA CHARANTIA DESCOURT

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Momordica charantia Descourt. belongs to the family Cucurbitaceae Juss. and it is locally known as Korola. *Momordica charantia* Descourt. is a common oriental vegetable with known communicable diseases and non-communicable diseases properties. This study investigates the effects of aqueous fruit extract of *Momordica charantia* Descourt. on the transport of D-glucose, L-tyrosine, electrolytes (Na^+ & K^+), and fluid across rat-everted intestine *in vitro*. The seasonal appearance and mucosal disappearance of D-glucose, L-tyrosine, Na^+, and the fluid absorptive capacity of the intestine were significantly inhibited ($p<0.05$) with increasing graded concentrations of *Momordica charantia* Descourt. The concentration of D-glucose accumulated or metabolized by the enterocytes in the intestinal tissues were significantly higher ($p<0.05$) when incubated with *Momordica charantia* Descourt.. Increasing graded concentrations of exogenous ATP (25-200 μM) were incubated with 3.0 mg/ml *Momordica*

charantia Descourt. to confirm inhibition of the ATP-dependent active transport of D-glucose, L-tyrosine, and fluid across rat enterocytes. It was found that increasing concentrations of mucosal ATP from 25 to 100 μM significantly ($p<0.05$) reverses the *Momordica charantia* Descourt.-depression of the D-glucose, L-tyrosine, and fluid uptake across rat everted intestinal sacs. Michaelis-Menten constant (K_m) and maximal velocity (V_m) were calculated in the presence and absence of *Momordica charantia* Descourt. fruit extract. It was observed that *Momordica charantia* Descourt. significantly reduced V_m of D-glucose uptake by 0.09 $mM.hr^{-1}$, whereas K_m remained unaltered suggested a non-competitive type of inhibition was present. It is hypothesized that bioactive phytochemicals such as saponins in *Momordica charantia* Descourt. fruit extract inhibits the active transport of D-glucose, L-tyrosine, and fluid across rat intestine by inhibiting the production of ATP thereby involving the Na^+ pump for the active transport of these molecules. It is likely that *Momordica charantia* Descourt. can be a potential alternative drug therapy of postprandial hyperglycemia via inhibition of glucose uptake across the small intestine.

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ANTIDIABETIC POTENTIAL OF STEM JUICE OF MUSA X SAPIENTUM LINN (SYN. MUSA X PARADISIACA LINN.) IN STREPTOZOTOCIN DIABETIC RATS

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Ethnopharmacological relevance:
Musa .X sapientum Linn. *(*syn. *Musa .X paradisiaca* Linn). is used in indian folk medicine for treatment of diabetes.

Aims and objective:
Antidiabetic effect of stem juice of *Musa .X sapientum* Linn. was studied in streptozotocin diabetic rats.

Materials and Method:
Rats were divided into five groups of six each. Group I healthy control, Group II healthy rats treated with stem juice (50mg/kg), Group III diabetic control, Group IV diabetic rats treated with stem juice (50mg/kg), Group V diabetic rats treated with standard drug Glibenclamide (0.6mg/kg). Effects of treatment was assessed on fasting blood glucose, postparandial bloodglucose, Total cholesterol (TC), Triacylglycerol (TAG),LDL+VLDL-Cholesterol(LDL+VLDL-C), HDLCholesterol(HDL-C), Glycosylated hemoglobin (GHb) and insulin.

Results:
Diabetic rats treated with stem juice showed significant decrease in fasting and Postparandial blood glucose, TC, TAG, LDL+VLDL-C, HDL-C, GHb ($p<0.05$). where as HDL-C and fasting serum insulin value increased in treated diabetic rats ($p<0.05$).

Conclusion:
Results of the study show that stem juice of *Musa. X sapientum* Linn. has significant antidiabetic effect.

Keywords:
Diabetes mellitus/ *Musa X sapientum* Linn, syn. *Musa X paradisiaca* Linn. stem / Antidiabetic effect.

STUDY OF SERUM LEVELS OF 25-HYDROXY VITAMIN D IN TYPE 2 DIABETIC PATIENTS IN RELATION TO CARDIOVASCULAR DISEASE

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Aim:
Evaluating the serum levels of 25- hydroxy vitamin D during the winter months in relation to cardiovascular disease in type 2 diabetic patients.

Subjects and Methods:
Eighty adult males were divided into: Control volunteers group (group I n = 15) and 65 Patients (group II) as: Group IIA (25) type 2 diabetic patients without cardiovascular complications. Group IIB(25) diabetic patients with cardiovascular complications. Group III(15) nondiabetic patients with stable ischemic heart disease (IHD).

Methods:
Physical examination, ECG, CIMT, plain x- ray chest, hands and pelvis, echocardiography, fasting, post prandial serum glucose, Hb A1c, kidney, liver and lipid profiles, CRP, fibrinogen, TBARs, PTH, 25(OH)D.

Results:
A significant decrease in 25(OH)D in the whole diabetic patients than in both control and IHD groups. Similarly, vitamin D was significantly decreased in Group IIB than in both control and IHDgroups.

Hypovitaminosis D showed the least value in diabetics with ischemic heart disease.

There was a negative correlation between 25 (OH)D, total cholesterol and LDL-C, diastolic and the mean blood pressure but it was not correlated with PTH, fibrinogen, CRP and TBARs.

Conclusion:
The significant decrease in 25(OH)D in diabetic patients than controls may throwing some light on its role in protection against diabetes.

Estimation of 25(OH) D in type 2 diabetic patients, is important to detect deficiency, the correction of which could be prophylactic against CVD complications.

Keywords:
cholecalciferol, vitamin D, parathormone, oxidative stress.

Abbreviations:
CIMT = carotid intima media thickness
TBARs = thiobarbituric acid reactive substances.
CRP = C-reactive protein
PTH = parathyroid hormone

ABNORMAL GLUCOSE TOLERANCE IN ADOLESCENTS WITH NEWLY DIAGNOSED POLYCYSTIC OVARY SYNDROME (PCOS)

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Context:
The exact etiology of PCOS is unclear; insulin resistance is shown to play an important role in development of the disease. Many studies have shown increased risk of insulin resistance among adults with PCOS irrespective of the body mass index (BMI). Data in the adolescent population is limited.

Objective:
To further understand insulin resistance in a small sample of newly diagnosed adolescents with PCOS.

Methods:
Retrospective chart review of female outpatients aged 10-19, newly diagnosed with PCOS, Eastern WI, USA.

Results:
103 cases were identified. The average age at diagnosis was 14.9 years. The mean weight, height, BMI, and BMI percentile from this cohort were 91.3kg, 165.2cm, 33.1 kg/m^2, and 93.5 respectively. Over 88% were classified as overweight or obese (≥85th percentile). Specifically, looking at 2-hour glucose levels from Oral Glucose Tolerance Tests (OGTT) only 41 cases had this value recorded; 24 normal (≤ 139 mg/dl), 15 impaired glucose (140 mg/dL-199 mg/dL), and 1 with diabetes (≥ 200 mg/dL). There was no difference in mean weight, height, or BMI when comparing those with impaired glucose tolerance to those with normal glucose tolerance. [Table 1] shows the characteristics of these groups. The only significant difference between these groups was a positive family history of diabetes (p=0.02) and higher level of free testosterone (p=0.01).

Conclusions:
These results suggest that impaired glucose tolerance may be independent of obesity in adolescents newly diagnosed with PCOS whereas family history of diabetes and hyperandrogenemia may be better indicators defining the risk in adolescents with PCOS.

GHRELIN IN OBESE TYPE 2 DIABETIC EGYPTIAN FEMALE PATIENTS

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Background:
it has been suggested that Ghrelin integrates hormonal and metabolic responses to stabilize fasting state glucose level and take part in the retention of lipids.

Aim:
Evaluation of the serum level of Ghrelin in obese Egyptian females with type2 diabetes mellitus.

Subjects:
Sixty adult females non pregnantand not taking contraceptive hormonal therapy were divided into: Group I ; fifteen healthy lean volunteers, Group 2; fifteen obese (BMI>30 kg/m^2) and Group 3 included thirty obese females with type 2 diabetes.

Methods:
Anthropometric measurements, thorough clinical examination, fasting serum glucose, hepatic and renal analytical evaluation and lipid profile, insulin and Ghrelin (at 0800h) were done. HOMA-IR and QUICKI indices were calculated.

Results:
QUICKI index showed significant decrease when each of obese controls and Type 2 diabetes groups, was compared to lean controls. Also, when obese controls were compared to obese diabetics, Ghrelin was relatively lower in the obese controls when compared to lean controls. A significant increase in Ghrelin level between obese patients with Type2 diabetes and obese controls. In patients with Type 2 diabetes, there was significant correlation between Ghrelin and ALT, HOMA-IR and QUICKI index.

Conclusion:
Insulin resistance, better identified by QUICKI index, is higher due to obesity alone than in patients with obesity and diabetes.

The significant increase in serum Ghrelin level detected between obese patients with Type2 diabetes when compared to obese controls group indicates that diabetes may cause elevation of basal serum Ghrelin .

Key words:
Ghrelin, insulin resistance, QUICKI index, Diabetes.
NB: HOMA-IR = Homeostasis Method Assessment
QUICKI index = Quantitative Insulin Sensitivity Check Index

METABOLIC DISORDERS AT FOLLOW-UP IN IRANIAN WOMEN WITH GESTATIONAL DIABETES MELLITUS IN PREVIOUS PREGNANCY

Background:
Pregnancy confers a state of insulin resistance and hyperinsulinemia that may predispose some women to develop diabetes and that fades away after delivery. GDM (Gestational Diabetes Mellitus) is defined as glucose intolerance of variable severity with onset or first recognition during pregnancy. GDM is one of the most frequent medical complications of pregnancy that affects between 1-14% of pregnant women. Women with prior GDM have an increased risk of later diabetes mellitus, abnormal glucose tolerance and cardiovascular risk factors and events. It is necessary to follow up patient with GDM in order to detect any Glucose intolerance and improve their long-term outcome.

The aim of the present study was to determine the prevalence of abnormal glucose tolerance and the metabolic disorders in a cohort of previously GDM women 1 year after delivery.

Materials and Methods:
In this study 116 patients with recent GDM were assessed 6- 12 months after delivery. Fasting Glucose, OGCT, lipid profile, and androgens were measured. Clinical and obstetrical history based on history of macrosomia, breastfeeding were assessed and analyzed statistically.

Results:
The result of this study shows %19.6 diabetes mellitus (DM) and % 16.2 impaired glucose tolerance test (IGT). In comparison with normal women, women with DM and IGT had higher blood pressure, waist circumference; lipid profile disorders such as high total cholesterol, LDL cholesterol, triglyceride and low level of HDL cholesterol were seen. There was a significant relationship between diabetes after delivery and high prevalence of hypertension.

Conclusion:
disturbed carbohydrate metabolism and a clustering of cardiovascular risk factors might be observed in previous GDM women 1 year after delivery.

Key words:
GDM ،metabolic disorders

DIASTOLIC DYSFUNCTION IN PERUVIAN OVERWEIGHT PATIENTS DIAGNOSED BY TISSUE DOPPLER IMAGING

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Introduction:
The information linking diastolic dysfunction and overweight is still limited. Although there are several investigations that have studied the effects of obesity on diastolic function, few of them have addressed the potential risk that slight elevations of the Body Mass Index (BMI) may have on diastolic function

Hypothesis:
Is diastolic dysfunction present in asymptomatic overweight subjects?

Methods:
A Tissue Doppler Imaging echocardiography as well as a conventional Doppler echocardiography were performed in 28 healthy, asymptomatic, peruvian participants between the ages of 18 and 59, and recruited in the years of 2007 and 2008. Overweight status was defined by a Body Mass Index ≥25 and <30 kg/m^2; participants with previous heart disease were excluded. According to the echocardiography, the diastolic function was classified in: normal, abnormal relaxation, pseudonormal and restrictive.

By both types of echocardiographic studies, we measured the E wave (early diastolic flow) and the A wave (auricular flow), at the mitral valve. Patients with findings consistent with diastolic dysfunction were further classified as: abnormal relaxation, pseudonormal and restrictive, based on the isovolumetric relaxation time, E wave deceleration time, and the systolic/diastolic speed ratio of the pulmonary veins.

Results:
The population studied had a mean age of 31.6, a male to female ratio of 5.6, and a mean BMI of 27.8. Using the Tissue Doppler Imaging as Gold Standard, a frequency of 28.6% of diastolic dysfunction was found in the participants, with a mean of 0.73 E'/A' ratio, opposed to the conventional doppler echocardiography which only identified as positive 7.1% of test subjects. Of the 28.6% found, the totality of it corresponded to the abnormal relaxation class. Additionally, we found a tendency for the E'/A' to be smaller as the BMI grew closer to 30 kg/m^2.

Conclusions:
In our series we found that 28.6% of the participants with overweight had diastolic dysfunction. There was a correlation tendency between the degree of overweight and the E'/A' index. We found Tissue Doppler to be the method with the highest yield for

the diagnosis of diastolic dysfunction. This study brings to attention the possibility of cardiac risk and morbidity from diastolic dysfunction in the overweight population.

ADIPONECTIN-RESISTIN AND INSULIN RESISTANCE INDEXES: THE NOVEL AND ROBUST PREDICTIVE INDEXES OF INSULIN RESISTANCE, TYPE 2 DIABETES, METABOLIC SYNDROME AND CARDIOVASCULAR DISEASE

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Introduction:
Hypoadiponectinemia and hyperrestinemia independently links insulin resistance to type 2 diabetes (T2DM) and metabolic syndrome (MS) which eventually increased the risk of cardiovascular disease (CVD). The aim of this study was propose a novel adiponectin-resistin (AR) index [$1+\log_{10}(R_0)–\log_{10}(A_0)$] by unifying the metabolic effect of adiponectin and resistin. Then, a novel insulin resistance (IR_{AR}) index [$\log_{10}(I_0G_0)+\log_{10}(I_0G_0)\log_{10}(R_0/A_0)$] was proposed by taking into account the AR index.

Methods:
The anthropometric clinical and metabolic parameters included serum adiponectin and resistin levels were determined in 809 Malaysian male subjects (208 controls, 174 MS without T2DM, 171 T2DM without MS, 256 T2DM with MS) whose ages ranged between 40-70 years old.

Results:
Adiponectin plays an important role in determining serum HDL cholesterol, triglycerides, and insulin levels. While, resistin plays a crucial role in determining plasma glucose and whole blood HbA1C levels. The AR index was stronger correlated with insulin resistance indexes and risk factors particularly serum insulin, plasma glucose and whole blood HbA1C levels rather than adiponectin and resistin alone. The AR index plays greater role in reflecting circulating metabolites levels rather than adiponectin and resistin alone. Moreover, the AR index showed stronger association with T2DM and MS susceptibility rather than hypoadiponectinemia and hyperrestinemia individually. The IR_{AR} index showed that hypoadiponectinemia and hyperrestinemia were strongly predisposing insulin resistance to T2DM and MS.

Conclusions:
The novel AR and IR_{AR} indexes are convenient, robust, potent and useful diagnostic biomarkers of insulin sensitivity for screening persons with increased risk of future development of T2DM, MS and CVD.

ADIPONECTIN-RESISTIN INTERACTION: HAPLOTYPE ADIPONECTIN AND RESISTIN IN LINKING INSULIN RESISTANCE TO TYPE 2 DIABETES AND METABOLIC SYNDROME

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Introduction:
Recent meta-analysis of genome-wide linkage and association studies have shown that haplotypes of adiponectin and resistin were associated with hypoadiponectinemia and hyperrestinemia, which eventually increased the risk of insulin resistance (IR), type 2 diabetes (T2DM), metabolic syndrome (MS) and cardiovascular disease (CVD).

Methods:
Real-Time PCR was used to genotype SNPs adiponectin (SNP+45T>G, SNP+276G>T, SNP+639T>C and SNP+1212A>G) and resistin (SNP-420C>G and SNP+299G>A) in 809 Malaysian male subjects (208 controls, 174 MS without T2DM, 171 T2DM without MS, 256 T2DM with MS) whose ages ranged between 40-70 years old. The genotyping results for each SNP marker was verified by sequencing. The anthropometric clinical and metabolic parameters of subjects were recorded.

Results:
Adiponectin-resistin interaction was stronger in linking IR to T2DM and MS rather than hypoadiponectinemia and hyperrestinemia individually. Haplotypes of adiponectin and resistin were strongly associated with their respective adipokine levels, as well as to the key metabolic endpoints of T2DM and MS. Haplotypes of adiponectin were strongly associated with hyperrestinemia, hyperglycaemia and hypertension. While, haplotypes of resistin were strongy associated with hyperrestinemia, hypoadiponectinemia and dyslipidemia. The haplotype combinations of SNP-420C>G and SNP+299G>A had greater impact than that of each SNP alone on serum resistin levels. The G-allele of SNP-420C>G when linkage disequilibrium with the A-allele of SNP+299G>A was stronger triggering hyperrestinemia. Adiponectin-resistin interaction might account for the functional links between haplotypes of adiponectin and resistin.

Conclusions:
Adiponectin-resistin interaction was strongly predisposing IR to T2DM and MS. Haplotypes of adiponectin and resistin were strongly linked to risk factors for IR, T2DM, MS and CVD.

AMELIORATION OF OBESITY AND ASSOCIATED METABOLIC DISORDERS IN DIET-INDUCED OBESE MICE BY SOLUBLE DIETARY FIBER HYDROXYPROPYL METHYLCELLULOSE

Shao-Ching Hung, W.H. Kerr Anderson, Dave R. Albers, Marsha L. Langhorst, and Scott A. Young

Dietary supplementation of the semi-synthetic soluble fiber hydroxypropyl methylcellulose (HPMC) has been reported to reduce body weight gain, postprandial glucose levels and lower plasma cholesterol. To investigate the utility of HPMC supplementation in healthy management of body weight and the manifestations of the metabolic syndrome, we examine the progression of weight, lipid and glucose metabolism in obese and diabetic C57BL/6J (B6) mice treated with high-fat (60% kcal), low-fat (10% kcal), and HPMC (4% and 8% w/w) in high-fat diets for five weeks. Significant weight loss in obese B6 mice was observed in 4% and 8% HPMC groups in a dose-dependent manner. In addition, significant decreases in adipose, liver weights, the concentrations of plasma cholesterol, and hepatic lipids were seen. A supplement of 8% HPMC in high-fat diet also resulted in significant improvements in glucose homeostasis, insulin sensitivity, and leptin concentrations. Reductions in plasma cholesterol, glucose, and insulin levels are strongly correlated with reduced leptin concentrations. Moreover, increases in fecal secretion of total bile acids, sterols, and fats indicated altered fat absorption when HPMC is incorporated in the diet. Collectively, our results suggest that HPMC not only reduces body weight but also normalizes the metabolic abnormalities associated with obesity and suggest that the effect of HPMC on glucose and lipid homeostasis in B6 mice is mediated through improvement in leptin sensitivity resulting from reduced fat absorption.

CARDIOMETABOLIC RISK FACTORS AND TESTOSTERONE LEVELS IN MEN: IMPLICATIONS FOR TESTOSTERONE SUPPLEMENTATION

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The association of metabolic syndrome or insulin resistance with low testosterone in men has led to interest in testosterone therapy to improve risk. Cardiometabolic risk markers were tested after overnight fasting in dried blood spots (DBS), and testosterone was assayed simultaneously in either DBS or saliva. After excluding samples with insulin >15 μIU/mL (to eliminate diabetics) or high-sensitivity C-Reactive Protein (hs-CRP) >10 mg/L (indicative of inflammatory disease not cardiometabolic risk), 228 samples were available for analysis. Samples were categorized (in tertiles) by testosterone level: low T (<300 ng/dL in DBS or <40 pg/mL in saliva); normal T (300-800 ng/dL DBS or 40-140 pg/mL saliva); and high T (>800 ng/dL DBS or >140 pg/mL saliva). Current testosterone therapy was self-reported in 1/20, 15/174, and 24/34 of the low, normal, and high T groups respectively; mean age (SD) was 54 (9.5), 50 (11), and 49 (13) respectively. Mean insulin was significantly higher in low T than either normal or high T men; hs- CRP was significantly higher in low T than high T men; HDL-cholesterol was significantly lower in high T than normal T men; and LDL-cholesterol was significantly higher in high T than low T men. Total cholesterol, triglycerides, and HbA1c were not significantly different between groups. Although over-supplementing with testosterone to supraphysiological levels may affect lipids adversely, normal or high testosterone levels were associated with favorable insulin and hs-CRP. Testosterone supplementation should be monitored to ensure levels remain in a physiological range for optimum cardiometabolic risk benefits.

OVEREXPRESSION OF HUMAN AKT1 TO GENERATES A NOVEL OBESITY MODEL IN ZEBRAFISH

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Recent evidences have demonstrated phosphatidylinositol3-kinase (PI3-K)/Akt signaling pathway participates in cell growth, cell survival, and adipocyte differentiation and lipogenesis *in vitro*. However, the *in vivo* evidence to support Akt function on adipogenesis is limited. To achieve this goal, we generated the stable zebrafish transgenics of Tg(*krt4:myrAkt1*)^{cy18} carrying human constitutive active form of Akt1 (myrAkt1) that driven by a skin-specific *krt4* promoter. At embryonic to larvae stages, Tg(*krt4:myrAkt1*)^{cy18} display severely skin hypertrophy but not hyperplasia supporting Akt1 function as a master gene on cell size control. Whole-mount immunostaining showed the exogenous human myrAkt1 is specifically expressed in the superficial skin layer. Western blot showed the Akt1 downstream targets like mTOR, GSK-3α/β and 70S6K are highly phosphorylated in Tg(*krt4:myrAkt1*)^{cy18}. After knocking down the protein expression level of mTOR or/and 70S6K by morpholino oligo injection, we are able to reverse the skin phenotype indicating the hypertrophic skin is primarily caused by Akt1 signaling overactivation. When transgenics reached sexual maturation, adipocytes display hyperplasia and hypertrophy and lead the transgenics to display lipoma-like obese phenotype. Whole body triglyceride and cholesterol measurement indicated the excess lipid is contributed by excess triglyceride storage. Interestingly, the excess lipid accumulation in Tg(*krt4:myrAkt1*)^{cy18}can be detected by Nile Red vital staining as early as from 21 hpf onwards. Real time RT-PCR confirmed the majority of adipogenesis-, lipogenesis-, and adipocytokine- as well as inflammation-related gene transcripts are highly upregulated in Tg(*krt4:myrAkt1*)^{cy18}. Moreover, when challenge fish with 5% glucose to elevate the blood glucose level, the obese transgenics display worse glucose tolerance than non-transgenic siblings. Collectively, our findings provided a direct evidence to support Akt play provital roles on cell size control as well as adipogenesis *in vivo*. In addition, the obese zebrafish line of Tg(*krt4:myrAkt1*)^{cy18} provide a new platform to study obesity, chronic diseases mechanism as well as perform *in vivo* anti-obesity drug screen.

LEPTIN -2548G/A AND -188C/A POLYMORPHISMS ARE RELATED WITH INFLAMMATION AND HEMATOPOIESIS IN MEXICAN OBESE CHILDREN

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Abstract

Leptin is a hormone involved in regulating appetite and body weight, but also has neuroendocrine functions in inflammation, immunity and hematopoiesis. Variants in leptin gene have been associated with serum leptin levels, obesity and an inflammatory state.

Aim:

To assess the association of leptin -2548G/A and-188C/A polymorphisms with inflammation and hematopoiesis in a sample of Mexican obese children.

Materials and methods:

Participants were 225 children with age range 6 to 13 years. Anthropometric, biochemical and hematological measurements were obtained by standard procedures. The determination of serum hsCRP levels was made by turbidimetry and genotyping of both polymorphisms was carried out by PCR-RFLP.

Results:

The genotype frequencies for the leptin -2548G/A polymorphism were: GG (30%), GA (51%) and AA (19%) The genotype frequencies for the leptin -188C/A polymorphism were: CC (91.6%), CA (7.6%) and AA (0.8%). The obese children had higher levels of serum leptin and hsCRP, as well as an increase in leukocyte, erythrocyte and platelet counts. Both GG+GA genotypes of SNP -2548G/A were associated with both serum leptin and hsCRP levels, and BMI. However leptin -188C/A polymorphism was not related to these variables. Leptin levels were associated with hsCRP concentrations, leukocyte and erythrocyte counts, BMI and obesity.

Conclusions:

Serum leptin levels are associated with obesity, BMI, waist circumference, skinfold thickness, serum hsCRP concentrations and both leukocyte and erythrocyte counts. Both GG+GA genotypes of leptin -2548G/A polymorphism are associated with obesity, BMI, waist circumference, skinfold thickness and serum leptin and hsCRP levels.

LIVER DISEASE STRUCTURE EXPLORED IN RUSSIAN FEDERATION NATIONAL-WIDE DIREG-L-01903 STUDY FOR NON-ALCOHOLIC FATTY LIVER DISEASE SCREENING

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Aim:

to assess liver disease nosologic structure in patients enrolled into the national population-based DIREG-L-01903 study for non-alcoholic fatty liver disease (NAFLD) screening. NAFLD is the primary source of the insulin resistance.

Methods:

In total of 30 787 primary care patients (56 % females, mean age 47.8±16 yrs) were enrolled into open multicenter national-wide prospective study. Careful clinical examination, serum biochemistry (including glucose, ALT, AST, γ-GT, lipid spectrum and hepatitis screening) and abdominal ultrasound diagnostics with precise liver, spleen and pancreas assessment and waist circumstence were performed in 30 754 patients.

Results:

NAFLD was found in 8215 (27) % of included patients. Within group with confirmed NAFLD liver steatosis was diagnosed in 80.3 %, steatohepatitis in 16.8 %, and cirrhosis in 2.9 % of patients. AST was increased ≥ 1.5 N in 2816 (9.2 %), ALT was increased ≥ 1.5 N in 3144 (10.2 %) of patients. In total, liver ultrasound examination revealed liver enlargement in 16.3 % portal hypertension in 0.5 signs of liver steatosis in 24.2 % signs of liver fibrosis in 2.3 signs of liver cirrhosis in 0.8 of total patients. Further meticulous clinical evaluation in tertiary medical centers enclosed liver diseases shown in Table.

Diagnosis	N (%) from a total of 30754	N (%) from pts with liver disease
NAFLD	8315 (27.0%)	8315 (71.6%)
Alcohol-induced liver disease	1608 (5.2%)	1608 (13.9%)
Viral hepatitis, total	1617 (5.3%)	1617 (13.9%)
Hepatitis C	281 (0.9%)	281 (2.4%)
Hepatitis B	176 (0.6%)	176 (1.5%)
Hepatocellular carcinoma	71 (0.2%)	71 (0.6%)
Autoimmune hepatitis	89 (0.3%)	89 (0.8%)
Inherent liver disease (including hemachromatosis)	111 (0.4%)	111 (1.0%)
Toxic/drug-induced liver disease	120 (0.4%)	120 (1.0%)

Conclusion:
NAFLD seems to be most prevalent liver disease estimating 27 % of screened patient, whereas viral hepatitis and alcohol-induced liver disease have prevalence of approximately 5 %.

URIC ACID (UA) INDUCES LIPID ACCUMULATION IN LIVER CELLS

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Hyperuricemia (HU) has been associated with metabolic syndrome and hepatic steatosis in several studies. Experimental HU was associated with fatty liver. Therefore, we examined the effect of UA on fat accumulation and in specific enzymes involved in fat metabolism in human hepatoma cells (HepG2).

HepG2 cells were cultured with uric acid (UA, 12 mg/dL) for 48 hr. Intracellular triglycerides, fatty acid synthase (FAS) and enoyl-CoA-hydratase-2 (ECoAH) expressions, as well as translocation of carbohydrate responsive element binding protein (ChREBP) were evaluated. UA induced a 20% increment in intracellular triglycerides; which was similar in magnitude as the induced by fructose (5 mM). Co-incubation of UA with fructose further increased TG synthesis, suggesting that UA derived from fructose contributed, at least partially, to further raise intracellular TG´s. UA dose dependently decreased the mitochondrial enzyme ECoAH, an essential enzyme for β-oxidation. On the other hand UA increased FAS, which is central in the pathway of the novo lipogenesis. In addition UA significantly increased the nuclear translocation of ChREBP, which is a strong regulator of FAS expression.These findings support that UA is acting to induce liver steatosis by at least two mechanisms: lowering the disposal of intracellular lipids by reducing the expression of ECoAH and through inducing the nuclear translocation of ChREBP with a secondary overexpression of FAS.

RISK FACTORS FOR NON-ALCOHOLIC FATTY LIVER DISEASE IN RUSSIAN FEDERATION IN NATIONAL-WIDE DIREG-L-01903 STUDY

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It is known that fatty liver is the important reason of insulin resistance and the complication of the DM.

Aim:
to assess the risk factors for non-alcoholic fatty liver disease (NAFLD) in Russian Federation in the national population-based DIGER study.

Methods:
In total of 30 787 primary care patients (56 % females, mean age 47.8±16 yrs) were enrolled into open multicenter national-wide prospective study. Careful clinical examination, serum biochemistry (including ALT, AST, γ-GT, lipid spectrum, glucose and hepatitis screening) and abdominal ultrasound diagnostics with precise liver assessment were performed in 30 754 patients.

Results:
NAFLD was found in 8215 (27) % of included patients. Within group with confirmed NAFLD liver steatosis was diagnosed in 80.3 %, steatohepatitis in 16.8 %, and cirrhosis in 2.9 % of patients. Of notice, only in 3.6 % of NAFLD patients (1.0 % in all population) the diagnosis has been established *before* DIREG-L-01903 program initiation, despite regular observations of participants in primary care centers. AST was increased ≥ 1.5 N in 2816 (9.2 %), ALT was increased ≥ 1.5 N in 3144 (10.2 %) of patients. In total patients population most frequent associated clinical conditions were arterial hypertension (42 %), dyslipidemia (38%), and abdominal obesity (36 %). In total NAFLD patients population following conditions has been found significantly more frequent: arterial hypertension (70 %), dyslipidemia (76 %) and hypercholesterolemia (69 %), $p < 0.001$ compared with total population. In patients aged from 18 to 29 years abdominal obesity was identified as risk factor, because in was found in 45 % NAFLD patients in comparison with 14 % of patients without NAFLD, $p < 0.001$. The significance of abdominal obesity as NAFLD risk factor is decreased with advanced age due to relatively higher prevalence of obesity in patients without NAFLD aged from 40 to 80 years. NAFLD was diagnosed in 64.3 % of patients with type I diabetes, 69.8 % patients with type II diabetes, 45.2 % of patients with arterial hypertension, 61.5 % of patients with obesity and in 66.9 % in those with metabolic syndrome.

Conclusion:
Taking into account high prevalence (27 %) of NAFLD in Russian Federation the attention should be given for NAFLD risk factors such as arterial hypertension, dyslipidemia and hypercholesterolemia in all age groups as well as abdominal obesity in patients younger than 39 years. Metabolic factors clustering might explore an important link between metabolic syndrome and NAFLD.

EFFECT OF POLOXAMER 407 ON NITRIC OXIDE PRODUCTION AND CELL VIABILITY IN LPS INDUCED RAW 264.7 MACROPHAGE CELL LINE

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Poloxamer 407 (P407) is a hydrophilic, non-ionic surface-active agent. Intrapertioneal injections will lead to hyperlipidemia and atherosclerosis and P407 gel formulations containing insulin or insulin nanoparticles is useful for the preparation of a controlled insulin delivery system. Nitric oxide is a mediator of autoimmune destruction of pancreatic beta cells in insulin dependent diabetes mellitus. NFκB is the major transcription factor responsible for the induction of iNOS gene expression by LPS in RAW 264.7 cells. Activated macrophages express iNOS that causes excessive NO production and lead to inflammation and tissue injury. Several studies suggest that NFκB activation is a key event early in the pathobiology of diabetes. Inhibition of NFκB activation prevents cytokine induced cell death in human islet cells. In this study, P407 was tested in vitro on viability and nitric oxide production in LPS activated RAW 264.7 macrophages cells. For this purpose, cells were incubated with different concentrations of P407 for 1 hour and stimulated with LPS for 20 hours. 0.1-1.6mM P407 inhibited the LPS induced NO production dose dependently ($p<0.001$). 3.2 and 3.7mM P407 decreased the cell viability ($p<0.001$). As a conclusion, P407 could inhibit the NO production via inhibition of NFκB and iNOS and to be used as an alternative for inflammation and diabetes.

INSULIN RESISTANCE CAN ALSO BE PRODUCED BY ENDOGENOUS SUBCLINICAL HYPERTHYROIDISM

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Since it is known that overt hyperthyroidism, in patients with Graves' Disease, may develop insulin resistance (IR), we were looking for similar effects when patients only undergo endogenous subclinical hyperthyroidism (SH).

Patients and methods:
Two groups of premenopausal women with normal weight, aging 18-55 yrs, were evaluated. The first group [G1] (n=12), has not received any treatment before the study, while the second group (n=40) was included as the control group [G2]. The G1 was composed by patients with SH as follows: 6 with very mild Graves' Disease, 3 with Plummer Disease and 3 with Hashi-Graves. In all these cases, circulating levels of total T3 and T4 were in the normal range, while serum TSH concentrations were low (x=0.12±0.1mU/ml). By the other hand, all the euthyroid women from the control group had normal TSH values (x=2.01±1.1mU/ml). Glucose and insulin were determined baseline and 120 minutes after a mixed meal test. Insulin sensitivity was assessed by HOMA-IR, QUIKI and ALOULOU indexes. Secretion by pancreatic b-cells was calculated by HOMA-B index.

Results:
Levels of baseline glucose (mg/dl) were: G1=93±9, G2=83±10. Post-prandial Glucose: G1=104±14, G2=86±16. Basal insulinemia (mUI/L): G1=15±4, G2=6±3. Post-prandial insulinemia: G1=69±36, G2=29±20. HOMA-IR: G1=3.4±0.9, G2=1.2±0.7. HOMA-B: G1=191±73, G2=140±101. QUICKI: G1=0.32±0.03, G2=0.38±0.01. ALOULOU: G1=2.9±0.1, G2=3.3±0.4. Total T3 (ng/dl): G1=150±15, G2=119±21. Total T4 (μg/dl): G1=9.5±1.69, G2=8.4±1.35. These results were showing, in G1, significant higher values of glucose and insulin, both at basal and post-prandial states, as well as the HOMA-IR, HOMA-B, and total thyroid hormones.

Conclusions:
For the first time, we are demonstrating that, like in overt thyrotoxicosis, the development of IR can also be observed in patients with endogenous subclinical hyperthyroidism.

AMELIORATION OF INSULINRESISTENCY IN A PATIENT WITH LADA AND VISCERAL ADIPOSITY DUE TO TREATMENT WITH A FIXCOMBINATION WITH METFORMIN AN VILDAGLIPTIN

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Introduction:
Worldwide there is a tremendous rise in incidence of Diabetes mellitus. The main forms of diabetes are diabetes due to lack of insulin (Typ1) and Diabetes due to Insuline resistence (Typ 2). A rare form of diabetes is LADA. In these patients the pathomechanism shows slow progression in the loss of betacell function due to autoimmune inflamation. Due to this pathology LADA patients are initially considered having Diabetes Typ 2 in their phenotype often descibed as Typ 2a (without obesity). There is a strong increase of visceral adiposity in this group of patients. Visceral adiposity is one of the main causes for insulin resistency. Therefore the incidence of cardiovasular diseases goes up. Pre-existing measures like life style modification and sports are often not succesful. This case report shows the effect of adding Vildagliptin and Metformin to an intensified Insuline Regime in a patient with prooved LADA.

Methodology:
In a 60-year-old lady with diagnosed LADA (IAA-Ab and GAD positive) and augmented thigh circumference of 100 cm, measured standadized at umbillical level in exspiration, Insuline resistency was measured due to HOMA IR. Then a fixed combination of Vildagliptin and Metformin (50 mg/1000 mg Bid) was added. During the observation period of 6 months there were measured in Insuline dosage, Insuline resistency, body weight, other cardiovascular risk factors and rate of hypoglycemia. There were no changes in life style and comedication over this observational period.

Results:
There was a notable reduction of the daily dose of Insuline with positive effects on visceral fatty tissue, measured by thigh circumference, hypertension and dyslipoproteinemia. without changing comedication. Due to our treatment the vicious circle of increasing in Insuline dosage followed by rise in body weight and worsening of hypertension, dyslipoproteinemia and the other metabolic parameters could be interrupted.

Conclusion:
This data shows that treating Insuline resistency in originally Insuline deficient patients can lead to a notable reduction of daily insulin dose and an amelioration of the other metabolic parameters.

MULTI-VESSEL CORONARY ARTERY DISEASE PATIENTS – A PROFOUNDLY INSULIN RESISTANT GROUP

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Background:
Insulin resistance is central to the pathogenesis of several important diseases such as diabetes and cardiovascular disease, particularly multi-vessel coronary artery disease (MVD).

Aims:
Measure whole body insulin sensitivity in patients with MVD awaiting coronary artery bypass graft surgery (CABGS).

Assess any differences in their metabolic parameters compared to diabetics.

Methods:
Subjects awaiting CABGS at St. Vincent's Hospital Melbourne were recruited and grouped as diabetic or non-diabetic (n=7 per group), and matched for age, sex and BMI. Pre-surgery, non-diabetic patients underwent assessment via hyperinsulinaemic-euglycaemic clamp. Fasting glucose, lipid profiles and HbA1C were recorded in both.

Results:
Non-diabetic CABGS patients were a highly insulin resistant population, average glucose clearance rate of 2.43 ± 0.77 mg/kg/min (normal ≈ 7 mg/kg/min). Additionally, non-diabetic CABGS patients showed no significant differences in lipid profile and fasting glucose compared to diabetics, despite not being clinically diabetic. As expected, diabetics were found to have a significantly higher HbA1C level (P=0.017) compared to non-diabetics.

Conclusions:
Patients with MVD awaiting surgery were highly insulin resistant using a gold standard test. The impact of insulin resistance in this population in terms of intra- and post-operative outcomes will be examined in an ongoing study.

ETHNIC DIFFERENCES IN INSULIN RESISTANCE AND THE METABOLIC SYNDROME

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Background:
The incidence of insulin resistance is increased in people of South Asian and African-Caribbean origin however the incidence of the metabolic syndrome in these groups is less clear; South Asians show dyslipidaemia and central obesity, but African-Caribbeans have a relatively cardioprotective lipid profile. Most investigations of ethnic differences have been cross-sectional and include differences in age and BMI. We characterised the metabolic syndrome in South Asians and African-Caribbeans compared with white-Europeans matched for gender, age and BMI.

Methods:
85 South Asian and 70 African-Caribbean healthy subjects were matched with healthy white-European controls for gender, age (±3yrs) and BMI (±3kg/m^2). BMI (kg/m^2), waist circumference (cm), body fat (%), fasting glucose, insulin, QUICKI and lipids were assessed.

Results:

	South Asian (n=85)	White-European (n=85)	*p*	African-Caribbean (n=70)	White-European (n=70)	*p*
Male/Female	34/51	34/51	-	20/50	20/50	-
Age (yrs)	**50** (39,57)	**47** (35,54)	NS	**44** (38,49)	**43** (37,50)	**NS**
BMI (kg/m^2)	**26.7** (24.2,30.2)	**26.7** (24.3,30.2)	NS	**30.4** (27.4,34.8)	**29.7** (27.1,35.2)	**NS**
Waist (cm)	**96.8** (89.0,104.8)	**93.8** (87.9,101.9)	NS	**98.8** (88.3,107.5)	**100.5** (89.5,113.0)	**0.001**
Systolic Blood Pressure (mmHg)	**127** (119,144)	**122** (114,134)	NS	**125** (119,138)	**130** (116,143)	**NS**
Body fat (%)	**32.9** (26.3,38.8)	**32.3** (26.0,39.8)	NS	**36.2** (30.4,44.5)	**37.6** (29.1,42.1)	**NS**
Fasting insulin (pmol/l)	**83.0** (55.6,111.3)	**60.3** (50.0,75.0)	**0.004**	**84.1** (58.9,116.0)	**65.3** (43.8,96.5)	**0.02**
Fasting glucose (mmol/l)	**5.3** (4.9,5.9)	**5.0** (4.8,5.4)	NS	**5.1** (4.8,5.5)	**5.1** (4.8,5.5)	**NS**
Total-cholesterol (mmol/l)	**5.40** (4.7,6.1)	**5.25** (4.60,6.20)	NS	**4.70** (4.20,5.40)	**5.30** (4.70,6.00)	**0.001**
HDL-C (mmol/l)	**1.20** (1.10,1.40)	**1.40** (1.21,1.73)	**0.01**	**1.20** (1.10,1.50)	**1.32** (1.13,1.60)	**NS**
LDL-C (mmol/l)	**3.28** (2.88,4.00)	**3.02** (2.59, 3.73)	NS	**2.92** (2.36,3.36)	**3.15** (2.54,3.74)	**0.03**
Fasting triglycerides (mmol/l)	**1.50** (1.13,2.01)	**1.35** (0.90,1.90)	NS	**0.80** (0.70,1.30)	**1.30** (0.96,1.91)	**<0.001**
QUICKI	**0.33 (0.31,0.35)**	**0.34 (0.33,0.35)**	**0.004**	**0.38 (0.36,0.40)**	**0.34 (0.32,0.36)**	**<0.001**

South Asians were more insulin resistant than Europeans and showed the characteristics of the metabolic syndrome. African-Caribbeans exhibited hyperinsulinaemia but were less insulin resistant than Europeans and had lower waist circumferences, total and LDL-cholesterol and triglycerides.

Discussion:
Cross-sectional studies have shown that South Asian and African-Caribbean populations are at increased risk of insulin resistance. We have shown, using a matched-pair design, this to be true for South Asians who show the classic metabolic syndrome profile. However African-Caribbeans appear to be less insulin resistant than white-Europeans matched for gender, BMI and age.

Conclusion:
These data suggest that the insulin resistance previously observed in African-Caribbeans is associated with obesity whereas in the South Asians the insulin resistant profile is apparent even under these controlled conditions and indicative of other genetic or environmental determinants.

ASSOCIATION OF CONGESTIVE HEART FAILURE AND BODY MASS INDEX WITH METABOLIC SYNDROME: 1999-2004 NHANES

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Several studies have now examined the association between metabolic syndrome and congestive heart failure (CHF); however, there is a paucity of studies examining CHF as a potential predictor of metabolic syndrome.

Purpose:
Examine the association of self-reported CHF as a potential predictor of metabolic syndrome and estimate the contribution of body mass index (BMI).

Methods:
Study sample included adults (N=3,830), 40 years and older in the 1999-2004 National Health and Nutrition Examination Survey. CHF was self-reported and BMI variables were measured in a medical examination center. SUDAAN was used for statistical analysis.

Results:
In men and women 40 years and older, the prevalence of CHF was 4.1% and 2.5% respectively between 1999 and 2004 in the United States. Participants with CHF were found to be 70% more likely to have metabolic syndrome (OR 1.70; 95% CI 1.10, 2.61) following adjustment for demographic variables and established risk factors. This association was attenuated following further adjustment for BMI. Our findings suggest that 15% of the association between CHF and metabolic syndrome was explained by BMI.

Conclusion:
Self-reported CHF was found to be associated with an increased likelihood of metabolic syndrome. Clinicians should understand

that an estimated 15% of the total effect of CHF on metabolic syndrome may be mediated by BMI.

RELATIONSHIP OF THE *HINDIII* AND S447X POLYMORPHISMS IN LPL GENE WITH HYPERTENSION AND DIABETES IN MEXICAN FAMILIES.

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Abstract

Several studies in families have demonstrated that genetic component play a central role to the development of the comorbidities associated to obesity, such as dyslipidemias, hypertension, type 2 diabetes (T2DM) and cardiovascular disease. Lipoprotein lipase (LPL) is a key enzyme in lipid metabolism and is associated with dyslipidemias. LPL gene polymorphisms can be related with the development of cardiovascular risk factors.

Aim:

Analyze the relationship of the *HindIII* and S447X polymorphisms in LPL gene with comorbidities in families with obesity.

Materials and methods:

Ninety members of 30 Mexican families, in which an index case had obesity, were included in the study. The families were integrated by case-parents trios. We evaluated the body composition by bioelectrical impedance. Peripheral blood samples were collected to determine biochemical parameters. Screening for *HindIII* and S447X LPL polymorphisms was performed by PCR-RFLPs

Results:

The genotype frequencies of *HindIII* polymorphism were 57.8% TT, 40% TG, and 2.2% GG. For the S447X polymorphism, the frequencies were 80% CC, 20% CG and 0% GG. In the parents, both polymorphisms were in Hardy-Weinberg's equilibrium. The genotype TT of *HindIII* was associated with diastolic blood pressure ≥ 85 mmHg (OR=1.1; p=0.011), whereas the genotype CC of S447X was associated with systolic blood pressure ≥ 130 mmHg (OR=1.2; p<0.001), diastolic blood pressure ≥ 85 mmHg (OR=1.3; p<0.001), T2DM (OR=1.3; p<0.001) and with increase of total cholesterol (β=23.6 mg/mL; *p*=0.03).

Conclusion:

The *HindIII* and S447X LPL gene polymorphisms can confer susceptibility for the development of hypertension and T2DM in Mexican families.

THE INFLUENCE OF NONALCOHOLIC FATTY LIVER DISEASE ON PLASMA LEVELS OF THE DISTANT MARKERS OF FIBROSIS AND IMMUNE INFLAMMATION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Type 2 diabetes mellitus (DM2) has been associated with an increased risk of nonalcoholic fatty liver disease (NAFLD). Insulin resistance is the main feature of hepatic fibrosis and cirrhosis. Collagen degradation is regulated by the condition of interstitial collagenases, in particular matrix metalloproteinases 1 type (MMP-1). It is necessary to determine levels of tissue inhibitor of metalloproteinases-1 (TIMP-1) and tumor necrosis factor-alpha (TNF-α) which regulate activity of MMP-1. Disturbing the balance between synthesis and degradation of collagen results in interstitial, reactive liver fibrosis.

Aim:

To study the dynamics of proMMP-1, TIMP-1 and TNF-α in patients with DM2 with- and without NAFLD.

Materials and methods:

Two groups of DM2 patients were investigated: first group included 30 DM2 patients without NAFLD, second group was 40 DM2 patients with NAFLD, and also 20 healthy persons were examined. The diagnosis of NAFLD was confirmed by histology and ultrasound. Criteria for diagnosing DM2 were consistent with WHO guidelines (1999). Plasma levels of proMMP-1, TIMP-1, TNF-α by ELISA method were studied.

Results:

Progressive and significant increase in levels of proMMP-1, TIMP-1, TNF-α, both in comparison with control group, and between groups, were revealed indicating increased severity of DM2 when accompanied by NAFLD.

Groups of patients	*Plasma levels*		
	proMMP-1, ng/ml	TIMP-1, ng/ml	TNF-α, pg/ml
Control group, n=20	1.4±0.05	373.0±1.6	22.8±1.4
DM2, n=30	2.0±0.096*	396.0±2.8*	40.1±1.6*
DM2+NAFLD, n=40	3.6±0.12*/**	442.0±2.4*/**	108.2±2.0*/**

* - vs control group (p<0.05)
** - DM2 vs DM2+NAFLD (p<0.05)

Conclusions:
increase of levels of proMMP-1, TIMP-1, TNF-α in DM2 patients were aggravated by damage of liver and contributed to clinical outcomes.

THE STUDY AND EVALUATION OF PLASMA LEVEL OF GHRELIN AND VISFATIN IN EGYPTIAN FEMALES WITH THE METABOLIC SYNDROME.

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Background:
The mechanisms underlying the metabolic derangements that occur in MS are not fully understood. How this is reflected on Ghrelin and Visfatin remains to be identified.

Aim:
Evaluation of the plasma levels of Ghrelin and Visfatin in MS in a trial to elucidate any contribution in the pathogenesis of this syndrome in Egyptian females.

Subjects and methods:
75 females divided into: 30 apparently healthy individuals divided into: 15 lean and 15 obese controls. The patients group included 45 patients having MS. Thorough history taking, anthropometric measurements, serum level of fasting glucose, insulin, creatinine, uric acid, lipid profile, ALT, BMI, waist-to-hip ratio and HOMA-IR, C-reactive protein, Ghrelin and Visfatin levels was also done.

Results:
CRP was significantly increased in obese controls and in patients when each group was compared to lean controls. Serum Ghrelin was significantly lower (P=0.015) in the obese controls as compared to lean control group. No significant difference in Visfatin level was detected between the studied groups. There was no significant correlations between Ghrelin, Visfatin and other studied parameters except significant negative correlation between Ghrelin and waist hip ratio in obese controls and significant negative correlations between Visfatin and both insulin and HOMA-IR in obese controls.

Conclusion:
1. There is a strong association between CRP and obesity in MS.
2. Serum Ghrelin level decrease with obesity in control subjects.
3. Visfatin is not related to anthropometric parameters and other parameters of MS.
4. Visfatin is associated with insulin sensitivity in women.

Key words:
Metabolic syndrome, Ghrelin, Visfatin.

THE METABOLIC SYNDROME PREDICTS ADVANCED SUBCLINICAL ATHEROSCLEROSIS AS ASSESSED BY CORONARY CALCIUM

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Background:
The metabolic syndrome is a risk factor for the development of coronary artery disease. However, the relationship between metabolic syndrome and advanced subclinical atherosclerosis as assessed by upper quartile (≥ 75th percentile) coronary artery calcium score (CACS) is not well described.

Methods and Results:
We evaluated the predictors of upper quartile CACS amongst 233 subjects (55% males and mean age of 53.9 years ± 10.6 yrs.; range 25 yrs. to 80 yrs.) in an asymptomatic screening population. The metabolic syndrome was defined with ≥ 3 of the following: waist circumference for men >40 inches and for women >35 inches; triglycerides ≥150 mg/dL; HDL cholesterol <40 mg/dL in men and <50 mg/dL in women; systolic blood pressure ≥130 and/or diastolic ≥ 85 mmHg or drug treatment for elevated blood pressure; fasting plasma glucose ≥100 mg/dL or drug treatment for elevated blood glucose. The prevalence of the metabolic syndrome and diabetes was 35.4% and 9.5%, respectively. In univariate analysis of 32 variables the metabolic syndrome ($p<0.001$ for all subjects and $p=0.004$ for those without diabetes), diabetes mellitus ($p<0.001$), fasting blood sugar ($p=0.01$), systolic blood pressure ($p=0.021$), cholesterol medicine use ($p=0.033$), and the Framingham risk score ($p=0.048$) were significantly related to upper quartile CACS. After adjusting for diabetes, fasting blood sugar, systolic blood pressure, and cholesterol medicine use, the metabolic syndrome was an independent predictor of upper quartile CACS [odds ratio 2.13 (95% CI 1.02-4.43)].

Conclusions:
As assessed by CACS ≥ 75th percentile, the metabolic syndrome is predictive of advanced coronary atherosclerosis.

TERMINALIA *ARJUNA* AS A THERAPEUTIC AND PREVENTIVE MODULATOR IN EXPERIMENTALLY INDUCED MYOCARDIAL INFARCTION

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Abstract

Cardiovascular disease, particularly ischemic heart disease (IHD) has become a worldwide health problem,and its prevention is a major public health challenge. Oxidative stress plays a potential role in CAD and it has been suggested to accelerate atherosclerosis. Terminalia *arjuna* (T.A) is traditionally used for the treatment of heart diseases. The present study demonstrates the effect of hydroalcoholic extract of T.A bark on oxidative stress markers and cardiac markers.

18 male albino rats of 150-200g, divided into three experimental groups (n=6).group I rats were given normal saline for 30 days, In group II normal saline was given to rats for30 days, Isoproterenol (ISP)85mg/kg b.w administered on 29th and 30th day. In group III rats were pretreated with hydroalcoholic extract of T. *arjuna* (HETA), for 30 days at a dose of 100,200 and 400 mg/kg b.w, ISP(85mg/kg b.w) administered on 29th and 30th day. oxidative stress markers and cardiac markers were evaluated. At the end of the study rats were sacrificed for histopathological examination.

HETA showed significant depletion in MDA, SGOT,CK-MB and Troponin I with a concomitant elevation in activity of SOD, GSH level($p<0.005$). Histopathology showed normal myocardium in gr.I, while in gr.II, patchy areas of necrosis, vacuolar changes with fragmentation suggestive of necrosis. Animals pre-treated with T.A (200mg/kg b.w)showed the maximal effect.

HETA(200mg/kg b.w) was found to be more effective in reduction of MDA,SGOT,CK-MB and Troponin I . The results suggest that HETA is effective in reducing the oxidative stress associated changes in cardiac enzymes,and augments endogenous antioxidant compounds of rat myocardium.

INDEPENDENT DISEASE MANIFESTATIONS OF COMMON RISK FACTORS: BRAIN WHITE MATTER LESIONS AND NONALCOHOLIC FATTY LIVER DISEASES

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Aim:

To investigate the association between Nonalcoholic Fatty Liver Diseases (NAFLD) and brain White Matter Lesions (WML) in slightly hypercholesterolaemic subjects.

Background:

NAFLD has been accepted as being the liver component of the metabolic syndrome (MetS) and the relation between NAFLD and cardiovascular disease is well established. Brain WML is an asymptomatic condition representing microvascular ischemic changes in the brain, indicating the presence of a fragile cerebral vascular network. Hence, white matter abnormalities are commonly seen in patients with risk factors such as hypertension, diabetes and hyperlipidemia. NAFLD patients have the same risk factors.

Methods:

A total of 172 subjects above 35-year old, with untreated hypercholesterolaemia , liver function test up to thrice the normal values and insignificant alcohol intake (below 20g/week) were screened for presence of NAFLD and WML, employing ultrasound and MRI respectively. Full blood chemistry was performed.

Results:

Out of 172 subjects screened 96 (55.81%) were diagnosed with NAFLD, with 54 (66.67%) out of 96 also positive for WML. In the NAFLD negative group (n=76), prevalence of WML was inversely distributed, with 34 positive (44.74%) and 42 (55.26%) negative findings. Subgroup analysis for subjects above 50-year (n=93), showed 57 (61.29%) of the subjects had NAFLD, of which 38 (66.67%) had also WML.

Conclusions:

The present study showed high prevalence of brain WML and NAFLD in hyperchoelsterolemic subjects. In particular, above 50-year old 2 out of 3 subjects with NAFLD have WML.

Independent disease manifestations of common risk factors: brain white matter lesions and nonalcoholic fatty liver diseases

DECREASED HOSPITAL STAY IN DIABETICS- DO STATINS HELP

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Background:

Clostridium difficile (C.diff.) colitis has been gradually increasing in frequency in the United States with worsening patient

outcomes. Diabetes has been shown to be a risk factor for C.diff colitis.

Methods:
We assessed factors associated with an increased length of hospital stay in patients with diabetes with C.diff colitis.

Results:
Over a period of 2 months, 20 inpatients had a diagnosis of C.diff colitis with diabetes. There were 8 males and 12 females in the study cohort. The mean age (± SD) was 69.4 ± 12.6 years with a mean (± SD) length of hospital stay of 12.2 ± 11.7 days. On assessing the factors associated with an increased length of stay, statin use was inversely correlated with length of hospital stay. On multivariate analysis, adjusting for insulin use, age and APACHE 2 scores, statin use (p=0.04) was the only factor which was significantly associated with a decreased length of hospital stay in diabetic patients with C.diff infection. In addition, though 70% of the patients met AACE guidelines for statin use, only about 50% of the patients were on statins.

Conclusions:
Though this study has a small sample size, it does highlight the association of statin use and decreased length of hospital stay in diabetic patients with Clostridium difficile infection. This study emphasizes the importance of aggressive use of statins in diabetics which may help in reducing economic burden and improving patient quality of life. Larger prospective studies are needed to confirm this beneficial association.

INSULIN RESISTANCE IS CORRELATED WITH ABDOMINAL AND SUBCUTANEOUS ADIPOSITY IN MEXICAN CHILDREN.

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Abstract
Studies in children have established that increase BMI is associated with a raise in insulin resistance. Currently, there is not strict definition for insulin resistance in children. We present frequency estimates of insulin resistance based on our proper definition.

Aim:
Analyze the relationship of insulin resistance with body adiposity and blood pressure in Mexican children.

Materials and methods:
Participants were 225 children, 108 girls and 117 boys, with age range 6-13 yr. Body weight was determinate with TANITA Model BC-553 body composition monitor and height with SECA stadiometer. The circumferences were measured by duplicate using a SECA diameter tape. The thickness of four skinfolds was measured using DYNATRON caliper, and blood pressure with aneroid sphygmomanometer (RIESTER CE 0124). Insulin resistance was defined as a HOMA-IR upper 75th percentile for all children (HOMA-IR >2.4).

Results:
Insulin resistance was found in 24.9% of the children. The insulin-resistant children had increased BMI; waist, hip and arm circumferences; the skinfolds thickness (tricipital, bicipital, subscapular and suprailiac), and both systolic and diastolic blood pressure than the group with insulin sensitivity. A correlation was found between insulin resistance and BMI (r=0.39, p<0.001); waist, hip and arm circumferences (r=0.39, p<0.001) and the four skinfolds (r=0.21 to 0.29, p<0.001). Insulin resistance was associated with obesity (OR=5.6, p<0.001), waist and arm circumferences (OR=13.6, p=0.002 and OR=11, p=0.007, respectively), tricipital and suprailiac skinfolds (OR=5.1, p=0.01 and OR=5.5, p=0.01, correspondingly).

Conclusion:
Insulin resistance was associated with central and subcutaneous adiposity in school-age Mexican children.

PERIOPERATIVE DYSGLYCAEMIA IN NON-DIABETIC CARDIAC BYPASS PATIENTS: STRONG ASSOCIATION WITH INSULIN RESISTANCE AND THE METABOLIC SYNDROME

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Background:
Metabolic Syndrome (MS) and Insulin resistance (IR) increase the risk of cardiovascular disease. Perioperative dysglycaemia reflects a state of IR and is associated with poor outcomes post cardiac bypass surgery (CBS).

Aims:
- Measure whole body insulin sensitivity (M value) in CBS patients and correlate with metabolic profile, baseline, peak intra-operative and average post-operative fasting blood glucose (FBG) levels.

- Compare mean M-Value in patients grouped by number of MS features.

Methods:
Non-diabetic CBS patients at St. Vincent's Hospital Melbourne were recruited (n=13). Each underwent hyperinsulinaemic-euglycaemic clamp. Metabolic and FBG parameters were measured. Pearson's r and two-tailed T-test were used (significance $P<0.05$) in data analysis.

Results:
This population is highly IR (average M-value= 3.27±1.43 mg/kg/min). The M-value correlated significantly with insulin (r=-0.578, $P=0.038$), HbA1c (r=-0.601, $P=0.030$), C-peptide (r=-0.662, $P=0.014$) however, not with baseline FBG. The M-value correlated significantly with peak intra-operative (r=-0.716, $P=0.006$) and average post-operative (r=-0.624, $P=0.03$) FBG levels.

A significant relationship exists between level of IR and number of MS features. 0-2 MS features give an average M-value of 4.0±2.0 versus 2.55±0.6 in those with 3-5 MS features ($P=0.030$).

Conclusions:
Non-diabetic CBS patients were highly IR. MS features were prominent; ≥3 features were significantly associated with greater IR. The level of IR correlated strongly with the degree of observed perioperative dysglycaemia. Importantly, the lack of correlation between insulin sensitivity and baseline FBG puts pre-diabetics at risk of non-detection using standard pre-surgical assessment.

COMBINED DOSAGE OF LORANTHUS MICRANTHUS (MISTLETOE) AND CYMBOPOGON CITRATUS (LEMONGRASS) IS A POTENT REMEDY FOR INSULIN RESISTANCE, DIABETES AND HYPERTENSION

The ethanolic leaf extract of Viscum album and lemon grass given i.p. produced a dose-dependent fall in blood sugar. Doses of 200 mg/kg and 400 mg/kg body weight produced significant ($p < 0.05$) lowering of blood sugar in fasted normal white albino rats and alloxanized rabbits respectively. The fasting blood sugar, measured in milligram per 100ml (mg%), in normoglycemic rats was reduced by 29.5% while in streptozotocinised rabbits, the blood sugar was reduced from mean value of 680 ± 8.3mg % at zero hour to 83 ± 7.2mg% at 4h.

In assesing the effects of the extracts on blood pressure, test doses (5-160mg/kg) below the LD50 value were selected and used to determine the effects of each dose of extract on the arterial blood pressure (BP) and heart rate of normotensive and hypertensive rats. The extract produced a dose-dependent depression of blood pressure and heart rate in both normo- and hypertensive rats. At doses of 5mg/kg and 160mg/kg, the extracts produced 9.87 + 3.6% and 558 + 8.1% depression of BP respectively, in normotensive rats while the corresponding values for the hypertensives were 4.6 + 2.2% and 44.7+ 5.5% respectively. The action of the extract was also mdose-dependent.

The mechanism underlying the observed hypoglycemic effect may be related to enhancement in peripheral utilization of glucose and increase in insulin secretion. Histological results suggested restorative (protective) effect of the extract on pancreatic islet cells. We hypothesise a non-adrenergic, non-cholinergic mechanism for the action of the extract on blood pressure.

IMPAIRED FASTING GLUCOSE: HYPERGLYCEMIA VERSUS HYPERINSULINEMIA

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Patients with impaired fasting glucose (IFG) and normal fasting glucose (NFG) are differentiated on the basis of fasting plasma glucose (FPG) concentrations. However, little is known concerning differences in glucose and insulin concentrations between these groups in response to daylong mixed-meals. This study was initiated to address this question in an experimental population consisting of subjects with IFG (n=154) or NFG (n=151). Breakfast (1/5 of daily caloric requirements) was provided at 8AM, lunch (2/5 of caloric requirements) was provided at 12PM, and blood was sampled before meals and hourly until 4PM for glucose and insulin concentrations. Insulin action was determined by measuring steady-state plasma glucose (SSPG) concentrations during the insulin suppression test (the higher the SSPG, the more insulin resistant the person). As expected, mean (±SEM) FPG concentrations were higher in IFG (105±1 vs. 88±1mg/dl, $p<0.001$). Fasting plasma insulin (FPI) concentrations were also higher in IFG (20±1 vs.15±1μU/ml, $p=0.003$). Interestingly, total integrated glucose responses to meals above FPG was not different between the two groups (83±9 vs. 85±5mg/dLx8hours, $p=0.66$), whereas total integrated insulin responses to meals above FPI was significantly greater in IFG (302±18 vs. 210±15μU/mlx8hours, $p<0.001$). Finally, SSPG concentrations were higher in IFG (213±5 vs.164±6mg/dl, $p<0.001$). These data demonstrate that individuals with IFG are more insulin resistant, with higher daylong insulin responses but comparable daylong glucose responses to meals. Thus, NFG and IFG differ by more than FPG concentrations, and IFG seems to be more distinguished by insulin resistance and daylong hyperinsulinemia than daylong hyperglycemia.

EFFECT OF MODERATE-FAT DIET COMPLEMENTED WITH GREEN TEA ON ANTHROPOMETRIC AND BIOCHEMICAL MARKERS, AND CARDIOVASCULAR RISK IN OBESE PATIENTS

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Introduction:
Obesity (OB) is a chronic degenerative disease, characterized by oxidative stress (EOX). OB represents a global health problem and is a risk factor for having high levels of oxidized low density lipoproteins (LDLox). LDLox levels are an useful marker for cardiovascular diseases. Therefore a moderate-fat diet complemented with green tea could prevent and control OB and its complications.

Objective:
Analyze the effect of moderate-fat diet complemented with green tea on anthropometric and biochemical markers, and cardiovascular risk in obese patients.

Methods:
This study is a randomized, controlled clinical trial. A total of 43 obese patients were divided in two groups, control group (n=20) and intervention group (n=23), instructed to consume a moderate-fat diet and a moderate-fat diet complemented with green tea, respectively; follow-up period was three months. Anthropometric and biochemical measurements were performed and analysis of LDLox levels; determinations were realized at baseline, 1st, 2nd and 3rd months post-intervention. The statistical analysis were performed with SPSS 10.0 ($p<0.05$ as significant).

Results:
In the follow-up period, we observed an improvement in anthropometric and biochemical measurements into both groups. The weight loss represents the 84.2% of fat mass in the intervention group *vs.* 48.9% in the control group. The intervention group showed significantly reduction of % fat mass, triglycerides (TGL), LDLox and insulin resistance *vs*. control group, while HDL increased ($p<0.05$).

Conclusions:
A moderate-fat diet complemented with green tea showed a reduction of LDLox and TGL, and an increase of HDL. The LDLox improvement represents a decrease of cardiovascular risk.

MODERATE-FAT DIET CONTRIBUTES TO INCREASE PLASMATIC ADIPONECTIN LEVELS IN SUBJECTS WITH OVERWEIGHT OR OBESITY, BUT WITHOUT ASSOCIATION TO ADIPONECTIN -11391G/A POLYMORPHISM

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Introduction:
Obesity and overweight has become a major health problem in world. Globally, Mexico occupies the second place in the prevalence of obesity. Adiponectin participate in the metabolism and regulation of glucose. The Single Nucleotide Polymorphisms -11391 G/A has been associated with circulating adiponectin levels. Allele A has been reported that increases transcriptional activity and plasmatic concentrations of adiponectin.

Objective:
Analyze the effect a moderate-fat diet on adiponectin levels and determine interindividual responses to diet according to the adiponectin -11393G/A polymorphism.

Methods:
80 subjects with BMI ≥25 kg/m^2 were recruited. The nutritional intervention consisted of 55% carbohydrates, 15% proteins, 30% lipids (<7% saturates fat). Before and after 8 weeks of implemented diet anthropometric and biochemical measurements were performed. The polymorphism was realized by PCR-RFLP's

Results:
The mean body weight of 86.1±18.0 kg and a mean age of 39.3±11.6 years. Eighty three percent of the participants were woman, 36.3% presented overweight and 63.7% obesity. The 60% presented insulin resistance (IR). The allelic frequency of adiponectin polymorphism was: 65% allele G and 35% allele A. The nutritional intervention showed beneficial metabolic effects: reduction of IR (-20%), abdominal obesity (-27.5%) and corporal composition changes (normal weight 0-6.2%; overweight 36.3-43.7%, obesity 63.9-49.9% at baseline to 8 weeks respectively); adiponectin levels increase at end intervention. The adiponectin levels showed a tendency to increase in A allele carriers.

Conclusions:
The moderate-fat diet contributes to increase adiponectin levels. There were no significant differences in anthropometric and biochemicals parameters according to adiponectin -113991G/A polymorphism.

EVALUATION OF ASSOCIATION BETWEEN OSA AND METABOLIC SYNDROME, INSULIN RESISTANCE AND HS-CRP

Abstract
Background:
Obstructive sleep apnoea (OSA) is an important medical problem that shares many cardiovascular risk factors with metabolic syndrome. This study aimed to evaluate the possible association of OSA severity with metabolic syndrome, Insulin resistance and Hs-CRP.

Methods:
We evaluated 90 subjects who suspected for OSA (54.92 years). Blood sampling was taken after 12 hours fasting for glucose, insulin, high-density lipoprotein (HDL)-cholesterol, triglycerides, high-sensitivity C-reactive protein (Hs-CRP), and then Overnight

polysomnograghy was done. Insulin resistance was assessed by the homeostatic model (HOMA) and metabolic syndrome was evaluated according to The National Cholesterol Education Program's Adult Treatment Panel III report (ATP III), and subjects categorized by OSA severity. We compared three groups: without OSA, mild OSA and moderate to severe OSA .

Results:
28 subjects hadn't OSA, 28 and 34 subjects had mild and moderate to severe OSA, respectively. Metabolic score was 3.29±1.21, 3.07±1.27 and 3.59±1.048 in subjects without OSA and mild OSA and moderate to severe OSA, respectively(r=0.13 p=0.22). HOMA index was 56.87 ±55.84, 106.42 ±199.68 and 96.23± 127.81 (r=0.33 p=0.37) and hs-CRP levels was 1.62±1.8, 2.10± 2.24 and 2.36±2.38 ng/ml(r=0.21 p=0.38) order in above three subjects. There was significant association between metabolic score and HOMA index (p=0.01) and also between metabolic score and hs-CRP level (p=0.02)

Conclusion:
Although Hs-CRP, insulin resistance and metabolic syndrome increase with OSA severity but there was not significant association between apnea hypopnea index and Hs-CRP, insulin resistance and metabolic syndrome.

SECRETION OF HMW ADIPONECTIN IS REDUCED IN VISCERAL BUT NOT SUBCUTANEOUS ADIPOSE TISSUE OF OBESE PEOPLE

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Objective:
Hypoadiponectinemia seen in obesity is associated with insulin-resistance, diabetes and atherosclerosis. We compared the release of adiponectin and its multimeric isoforms in explants derived from subcutaneous (SAT) and visceral adipose tissue (VAT) in obese and lean subjects.

Design:
Paired samples of SAT and VAT and blood samples were obtained from 24 subjects (10 lean and 14 obese). Total adiponectin quantities and adiponectin isoforms were measured using ELISA and non-denaturing Western blot, respectively.

Results:
The relative amount of high molecular weight form (HMW) of adiponectin to total adiponectin was higher in explant media of both depots than in plasma (by 19.7% in SAT and 23.9% in VAT, p<0.001). The release of total adiponectin was lower in obese than in lean subjects in both fat depot. In both, SAT and VAT explants, the most abundant isoform released into culture media was the HMW form. Ratio of HMW/total adiponectin in the explants medium was higher in VAT than in SAT in the group of lean (49.3% vs. 40.6%, p<0.01) while no difference was found in obese subjects (45.6% in VAT vs. 44.8% in SAT).

Conclusion:
The profile of adiponectin isoforms secreted by SAT and VAT explants differs from the plasma profile. The results show that relative proportion of the release of the biologically active HMW form is reduced in VAT of obese subjects. This suggests an impairment of the HMW secretion in VAT in obesity.

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COLESEVELAM SIGNIFICANTLY REDUCES LOW-DENSITY LIPOPROTEIN PARTICLE CONCENTRATION IN PATIENTS WITH PREDIABETES AND HYPERCHOLESTEROLEMIA

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Treatment guidelines recommend reducing low-density lipoprotein cholesterol (LDL-C) levels to <100 mg/dL in patients with prediabetes to reduce cardiovascular risk. However, studies suggest that patients with well-controlled LDL-C levels may still have elevated cardiovascular risk due to high concentrations of LDL particles (LDL-P). A 16-week, randomized, double-blind,

placebo-controlled, multinational study evaluated the effect of colesevelam on the concentration and size of various lipoprotein particles, as determined by nuclear magnetic resonance spectroscopy, in patients with prediabetes and hypercholesterolemia (LDL-C ≥100 mg/dL). Patients were randomized 1:1 to colesevelam 3.75 g/day (n=108) or placebo (n=108). At baseline, 6 patients (colesevelam group) and 10 patients (placebo group) were on statin therapy. LDL-C, non–high-density lipoprotein cholesterol (Non–HDL-C), and apolipoprotein (Apo)B levels significantly decreased from baseline with colesevelam (treatment difference [TD]: –15.6%, –9.1%, and –8.1%, respectively), whereas triglyceride levels significantly increased from baseline (TD: 14.3%; all $P<0.001$ vs placebo). In addition, colesevelam significantly reduced total LDL-P concentration (TD: –112.7 nmol/L; $P<0.05$ vs placebo), with no significant change in LDL-P size (TD: –0.11 nm). Although total very–low-density lipoprotein particle (VLDL-P) concentration was unchanged with colesevelam (TD: 1.53 nmol/L), VLDL-P size significantly increased (TD: 5.31 nm; $P<0.001$ vs placebo). The change in total high-density lipoprotein particle (HDL-P) concentration was similar between the treatment groups at study end; however, HDL-P size significantly increased with colesevelam (TD: 0.10 nm; $P<0.01$ vs placebo). In patients with prediabetes and hypercholesterolemia, colesevelam improved the overall atherogenic lipoprotein profile by significantly reducing LDL-C, Non–HDL-C, ApoB, and LDL-P concentrations.

INSULIN RESISTANT SUBJECTS DISPLAY ALTERED EXPRESSION OF GENES INVOLVED IN INFLAMMATION, MITOCHONDRIAL FUNCTION AND LIPID METABOLISM IN ADIPOSE TISSUE

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To gain insight into molecular mechanisms underlying insulin resistance, we compared acute in vivo effects of insulin on transcriptional profiles of insulin-resistant and -sensitive women. Subcutaneous adipose tissue biopsies were obtained before and after 3 and 6 h of intravenously maintained euglycaemic hyperinsulinaemia from 9 insulin-resistant and 11 insulin sensitive females. Gene expression was measured using Affymetrix HG U133 Plus 2 microarrays and qRT-PCR. Microarray data analysis and pathway analysis were performed with Chipster v1.4.2 and by using an in-house developed nonparametric pathway analysis software. Inflammatory pathways with complement components (inflammatory response, GO:0006954) and cytokines (chemotaxis, GO:0042330) were strongly upregulated in insulin-resistant as compared to insulin-sensitive subjects both before and during hyperinsulinaemia. The most striking difference in gene expression of the insulin-resistant group during hyperinsulinaemia was reduced transcription of genes involved in mitochondrial respiration (mitochondrial respiratory chain, GO:0001934). Furthermore, differences were observed in genes contributing to fatty acid, cholesterol and triglyceride metabolism and to regulation of lipoprotein lipase activity between the insulin-resistant and -sensitive subjects both before and during hyperinsulinaemia. The major finding of this study is defective induction of mitochondrial respiratory and lipid metabolism pathways upon hyperinsulinemia, in the insulin-resistant subjects. Moreover, the study reveals several new individual genes whose aberrant regulation is associated with the insulin-resistant phenotype.

LEPTIN IS A POTENTIAL EARLY BIOMARKER FOR CARDIOMETABOLIC RISK OF ADOLESCENTS

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Introduction:
Obesity is an important problem of Public Health and adipokines have a great impact in relation atherosclerosis *versus* obesity.

Objective:
To investigate the association of leptin and adiponectina with cardiometabolic risk of obese adolescents.

Materials and Methods:
Puberal adolescents (both sexes, 10-19 years old) were included. Lipid profile, glucose and insulin (commercial kits), leptin and adiponectin (ELISA), LDL(-) and its autoantibodies (ELISA) were monitored. Anthropometric (weight, height, waist circumference, fat percentage) were collected.

Results:
Linear trend analyses showed that the lower quintiles of leptin (5.8-40.6 ng/ml) were proportionally associated with waist circumference (72-101 cm; $P<0.001$), body mass index (21-35 kg/m^2; $P<0.001$), fat percentage (13-35%; $P<0.001$), insulin (13-28 μUI/ml$P<0.001$), HOMA-IR (2.7-5.7; $P=0.001$) and triglycerides

(70-96 mg/dl; *P*=0.019). Adiponectin did not show any associations with cardiometabolic risk.

Conclusions:
Leptin is a potential early biomarker for cardiometabolic risk in adolescent.

ACUTE INDUCTION OF INSULIN RESISTANCE WITH GLUCOSAMINE INFUSION INCREASES PANCREATIC ISLET BLOOD FLOW IN ANESTHETIZED RATS

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Conditions with increased demands for insulin secretion, including experimental type 2 diabetes, is associated with increased pancreatic islet blood perfusion. The mechanisms are mainly neural, but also locally formed products, such as nitric oxide, are involved. To what extent high blood flow affects islet function has been difficult to study. The aim of this study was to evaluate if an acutely increased peripheral insulin resistance induces an islet blood flow increase. This would enable us to further study the mechanisms and functional consequences of this on islets.

Anesthetized Sprague-Dawley rats were infused with glucosamine (6 mg/kg/h) or saline for 120 minutes. After 2h blood glucose concentrations were unaffected whereas serum insulin concentrations were almost doubled. Pancreatic islet blood flow, measured with microsphere technique, was higher in glucosamine-infused rats than in control rats, whilst the other organ blood flow values were unaffected. The normal glucose-induced increase in islet blood flow was unchanged after glucose administration, whereas subcutaneous fat blood flow was diminished compared to control animals. The reactivity of islet arterial smooth muscle cells, studied in single-islet perfusion system, was higher in glucosamine-infused rats.

Acute glucosamine-infusion leads to insulin resistance and this leads to selective increase in pancreatic islet blood flow. This model may be used to further explore the regulation of islet blood perfusion during impaired glucose tolerance.

EARLY INSULIN TREATMENT ALLEVIATES CHRONIC ADVERSE CHANGES IN POST-ISCHEMIC CARDIAC STRUCTURE AND FUNCTION

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Aim:
Insulin has been shown to possess significant cardioprotective effect in acute myocardial ischemia/reperfusion (MI/R). However, the role of insulin treatment on the prolonged cardiac remodeling and function in the ischemic heart remains unclear. The present study was aimed at investgating the effect of early and late insulin treatments on the prolonged post-ischemic cardiac structural and functional changes.

Methods:
Adult male rats were subjected to left anterior descending coronary artery occlusion and were randomized to receive one of the following treatments: saline, early insulin treatment or late insulin treatment (the same dose and routine of insulin starting at 1 wks after the ischemia surgery).

Results:
MI rats receiving early insulin treatment showed a smaller LV cavity compared with those in the saline-treated animals, and increased cardiac ejection fraction 4 wks after ischemia. However, compared with those of vehicle, late treatment with insulin had no effect on post-ischemic cardiac structure and function with both LV cavity and ejection fraction changed insignificantly 4 wks after ischemia. Interestingly, insulin-stimulated fluorodeoxyglucose uptake was 81.5% lower together with blunted Akt phosphorylation in noninfarcted myocardium 1 wk after ischemia compared with those in the normal animals, suggesting myocardial insulin resistance at this stage and reduced myocardial insulin responsiveness may be one possible mechanism that abolished the effects of late insulin treatment on cardiac structure and function.

Conclusions:
These data suggest that early, but not late, insulin treatment retards the subsequent development of ischemic heart failure in rat MI model.

METABOLIC PREDICTORS OF INSULIN SENSITIVITY PREDICT PROGRESSION TO IMPAIRED GLUCOSE TOLERANCE

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Insulin resistance is a risk factor and predictor of type II diabetes and cardiovascular disease. An unmet medical need exists to have a simple, practical measurement of insulin sensitivity in order to identify high-risk, insulin-resistant patients for more effective lifestyle intervention and disease prevention. We previously identified biomarkers of insulin sensitivity in a cross-sectional analysis of subjects in a non-diabetic, healthy population (n=399) (*Gall et al. PLoS One* (2010)), based on their highly significant correlations to the glucose disposal rate as measured by the gold-standard hyperinsulinemic euglycemic clamp. Herein, we describe selection of these top-ranking biomarkers as predictors of insulin sensitivity, and their incorporation into an algorithm developed from an expanded analysis of the entire EGIR-RISC nondiabetic cohort. In this random, nondiabetic population (n=1277), variable selection, absolute quantitative measurement, and log transformation of the key analytes, including a hormone, organic acid, acylglycerophospholipid, and fatty acid, resulted in a receiver operating characteristic (ROC) curve or AUC of 0.86 and 0.85 for identification of the bottom quintile and tertile of insulin sensitivity, respectively ($p<0.001$). Selection of these variables and their inclusion in a multivariate algorithm comprises the diagnostic development of a fasted blood test for insulin resistance, Quantose™ IR. Using 3 -year follow-up data on a large subset of the baseline EGIR-RISC subjects, we compared the predictiveness of the euglycemic clamp and the said predictor variables for clinical progression of subjects from normal glucose tolerance (NGT) to impaired glucose tolerance (IGT) (n=880), a state of worsening insulin resistance and dysglycemia. This multivariate algorithm predicting insulin sensitivity was statistically equivalent to the euglycemic clamp's predictiveness of subjects progressing from NGT to IGT (AUC=0.70), thus demonstrating clinical utility of the Quantose IR test. In conclusion, we demonstrate that a panel of insulin sensitivity analytes can identify high-risk insulin resistant subjects with high accuracy and predict worsening of beta cell deterioration, or progression to IGT, in the context of predicted insulin resistance status.

NOVEL MECHANISM OF ISCHEMIC PRECONDITIONING-INDUCED CARDIOPROTECTION: SWITCHING MYOCARDIAL SUBSTRATE UPTAKE TO GLUCOSE VIA INSULIN-DEPENDENT PI3K/AKT SIGNALING

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Objective:
One of the heart responses to stress is to switch myocardial substrate metabolism to increase energy efficiency. The present study was designed to investigate whether ischemic preconditioning (IPC) afforded cardioprotection through transition of increased myocardial glucose utilization and the underlying "switch" mechanism.

Methods:
Adult male rats were subjected to 30 min of myocardial ischemia and 3 h of reperfusion (MI/R). IPC was achieved by two cycles of 5-min occlusion and 5-min reperfusion. Myocardial glucose uptake was assessed at the end of 1 h reperfusion with ^{18}F-2-deoxy-2-fluoro-D-glucose using in vivo positron emission tomography and in vitro gamma-counter biodistribution.

Results:
IPC improved cardiac functional recovery and reduced myocardial injury following MI/R ($P<0.05$). Cardiac glucose uptake was markedly elevated after IPC treatment (17.0±1.5 vs. 12.4±1.0 in MI/R group, $P<0.05$, n=10-12), together with the increase in translocation of glucose transporter 4 (GLUT4) to cardiomyocyte membrane ($P<0.01$). Meanwhile, myocardial PI3K expression, Akt and glycogen synthase kinase (GSK)-3β phosphorylation were all significantly enhanced in IPC group ($P<0.05$). Wortmannin not only abrogated the cardioprotective effect of IPC, but also inhibited IPC-stimulated GLUT4 translocation. Moreover, the cardioprotection of IPC was markedly blunted in STZ-induced diabetic hearts with decreased GLUT4 translocation and impaired IPC-stimulated PI3K-Akt-GSK-3β signaling ($P<0.05$, n=6), suggesting that the impaired insulin signaling and subsequent failure of increase in glucose uptake blunts the cardioprotection of IPC in the diabetic hearts.

Conclusions:
These results suggest that IPC-induced transition of myocardial substrate uptake from fatty acids to glucose via insulin-dependent PI3K/Akt signaling contributes to IPC-induced cardioprotection.

Keywords:
ischemic preconditioning; glucose uptake; insulin signaling; Akt; cardioprotection

ACHIEVING ABCS OF DIABETES CARE WITH A "TEAM OF 4" APPROACH

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Background:
ADA recommends ABC goals: A1C <7%, Blood pressure < 130/80mmHg, and cholesterol (LDL) <100mg/dL. NHANES reports ~ ½ patients reach individual ABC goals; <12% achieve all 3. We evaluated the "team of 4" approach on ABC goal attainment and adherence to ADA guidelines.

Methods:
Retrospective evaluation conducted on adult diabetic patients seen by "team of 4" approach (defined as involvement & accountability

of physician, staff, patient, and family). Primary outcomes evaluated were clinical goal attainment (A1C, blood pressure, and LDL goals). Secondary outcomes included guideline adherence. Data were analyzed by paired t-test.

Results:
396 patients were included. Average age = 52 ± 15, 59% female, duration of diabetes = 12.6 ± 9.3 years. Primary outcomes showed 49.5% of patients achieved A1C goal at baseline vs 50.8%(1yr), 51.3%(2yr), 49.0%(3yr), 40.9%(4yr), and 39.9%(5yr) ($p<0.05$ for years 1 & 2 vs baseline). Blood pressure goals were attained in 45.7% at baseline vs 58.6% (1yr), 61.4% (2yr), 61.6% (3yr), 64.1%(4yr), and 62.4% (5yr) ($p<0.05$ for all). LDL goal attainment was 35.6% at baseline compared to 62.6%(1yr), 59.1%(2yr), 61.9%(3yr), 58.8%(4yr), 56.8%(5yr) ($p<0.05$ for all). All 3 goals were attained in 6.1% at baseline versus 21.7%(1yr), 23.2% (2yr), 22.0%(3yr), 20.2%(4yr), and 16.9%(5yr) ($p<0.05$ for all). Secondary outcomes demonstrated significant improvement in the % of patients on statins ($P<0.05$ vs baseline for each) and % of patients receiving appropriate cholesterol laboratory monitoring ($P<0.05$ vs baseline for each).

Conclusions:
The "team of 4" approach has a positive benefit on achieving patient goals and adhering to evidence-based guidelines.

RELATIONSHIPS BETWEEN LIVER FAT, CIRCULATING ADIPOCYTOKINES AND INSULIN RESISTANCE IN OBESE HISPANIC ADOLESCENTS

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Background:
The aim of this study was to identify metabolic markers most highly associated with elevated liver fat in obese Hispanic adolescents.

Methods:
Forty-one obese Hispanic adolescents (15.3±1.0 years, BMI: 97.0 ± 3.9 percentile) were assessed for: visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) and hepatic fat fraction (HFF) by MRI; fasting measures of serum glucose, insulin, and adipocytokines including adiponectin, plasminogen activator inhibitor-1, leptin, monocyte chemoattractant protein-1, interleukin-8 (IL-8), nerve growth factor (NGF), hepatic growth factor, resistin, and tumor necrosis factor-alpha; and insulin sensitivity (SI) and the acute insulin response to glucose (AIR) by IVGTT. Subjects with normal levels of HFF (below 5%; n = 25) were compared to those with HFF >5% (n = 16).

Results:
The 2 groups differing in HFF were similar for total body fat, VAT and SAT. The group with HFF >5% had significantly higher IL-8 (6.1 ± 1.6 vs. 3.2 ± 0.4 pg/mL), NGF (30.2 ± 9.9 vs. 13.9 ± 1.6 pg/mL), HOMA-IR (8.8 ± 1.1 vs. 5.5 ± 0.5), AIR (1869 ± 206 vs. 1092 ± 165), and a tendency for lower SI (1.2 ± 0.4 vs. 2.1 ± 0.3; p=0.06), with no significant differences in any of other factors measured.

Conclusions:
These data suggest that elevated liver fat is most closely associated with elevated serum IL-8 and NGF levels as well as increased AIR and HOMA-IR. These elevated factors may play significant roles in the metabolic abnormalities associated with elevated liver fat in obese Hispanics.

DEFIANCE OF *TRIDAX PROCUMBENS* L. ON THE SUCROSE INDUCED INSULIN RESISTANCE MEDIATED MUSCLE PROTEIN BREAKS DOWN IN RATS.

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Introduction:
The regulatory action of insulin on protein metabolism is well knows. In uncontrolled diabetes mellitus accelerated loss of muscle mass through decreased protein synthesis and increased protein degradation. In this conditions that activate the ubiquitin-proteasome system to cause muscle atrophy, which suggests that a common pathway of muscle proteolysis is present.

Purpose:
In many cultures with emerging epidemics of diabetes, traditional herbs have more acceptance than prescription drugs. *Tridax procumbens* is a proven antioxidant, antilipidemic, hypoglycemic and hypotensive herb. Hence this study aims at the defiance of *Tridax on* insulin resistance mediated muscle protein breaks down in rats.

Material:
In the male albino Wistar rats (95 to 110 gm) insulin resistance was induced by 32% sucrose solution. The various forms of *Tridax*, 1.entire leaf 2.alcoholic extract of leaf 3.ashed form of leaf were used as drugs.

Method:
The animals were divided into 8 groups. The sucrose solution and the three different forms of *Tridax* were given for 10 weeks. The

insulin and testosterone levels were estimated in the serum. In muscle protein, lipids, glycogen, antioxidant enzyme and thiobarbituric acid reactive substance (TBARS) were estimated, muscle proteins were separation by SDS-PAGE.

Results:
The increased body weight, elevated levels of serum insulin, muscle total lipids and TBARS, reduced antioxidant enzymes in muscle, decreased serum testosterone and muscle protein, glycogen were observed in sucrose fed animals. In the muscle proteins density were drastically decreased. All the three forms of *Tridax* restored the above changes. The best is the native and ashed form.

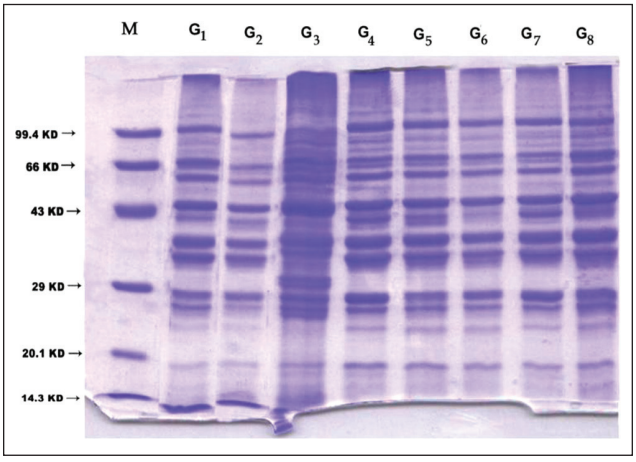

Plate.1. Muscle protein profiles of the different experimental groups
M- Marker G_3-Native *Tridax* G_6- Sucrose+ Extracted *Tridax*
G_1- Control G_4-Sucrose+ Native *Tridax* G_7- Ashed *Tridax*
G_2- Sucrose G_5-Extracted *Tridax* G_8- Sucrose + Ashed *Tridax*

Conclusions:
Tridax (all forms), especially native and ashed form exhibits defiance of sucrose induced insulin resistance mediated muscle protein break down. *Tridax* (free of residual toxicity) can be safely included in the diet for the early prevention of the diet induced insulin resistance mediated muscle protein break down.

ENVIROMENTAL PREDICTOR OF METABOLIC SYNDROME

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Background:
Metabolic Syndrome is well documented in epidemic proportions in the developed Countries. However, it`s scourge is now extending at an alarming rate to the developing Countries like Nigeria. There is a massive movement of people from the rural to urban centers with its associated Westernization which is taking a hard toll on Nigerians' metabolic profile. This study was designed to establish the effect of different environments (rural and urban) on two native Nigerian population with the same genetic composition, but exposed to different environmental factors .

Materials and methods:
Abuja is the new capital city of Nigeria mainly inhabited by the tribe of "Gbagi" before it became the country's capital about 18years ago. Some of the "gbagis" have been engulfed by urbanization while others, about 4,000 kilometers away are still living a village life. The study recruited 342 people (165men, 177women) from the "Gbagi tribe who live in the urban area of Abuja and 325 (171men, 154 women) also of the gbagi tribe who still live in the rural area, to establish the effect of the different environment factors on their metabolic indices. Research approvals were obtained from Benue State University, Abuja Municipal and Kuje Area Council ethical committees. Individual consent was also obtained from each subject.

Blood pressure was obtained using Mercury Sphygmomanometer, Skinfold thickness using Vennier Caliper, weight by using electronic weighing scale. All these were done according to WHO guidelines for such assessment.

Results:
The mean values for the fasting plasma glucose and anthropometric indices were significantly higher among the urban subjects than the rural subjects (fig 1). About 2.6% of the urban subjects had impaired fasting glucose (IFG) and Diabetes as against 0.6% among the rural subjects ($p<0.05$). More subjects from the urban had systolic and diastolic hypertension as against the rural subjects respectively (22% vs 13%; 15% vs 8%). In addition, about 44% of the urban subjects were overweight and obese as compared with 19% of the rural subjects ($P<0.05$). Serum triglyceride was significantly higher, while HDL cholesterol was significantly lower among the urban subjects compared with the rural subjects. However, there were no significant differences among both groups in relation to Total cholesterol and LDL cholesterol.

Conclusion:
Obesity, both localized and generalized is a forerunner of metabolic syndrome often caused by reduction in physical activities and increased caloric intake; Urbanization and Westernization are the major predisposing factors. This study established the strong link between metabolic syndrome and urbanization.

ANTIHYPERGLYCEMIC ACTIVITY OF VMNS2E, A NOVEL BIPHENYL PTP1B INHIBITOR AND ITS EFFECT ON INSULIN RESISTANCE, DIABETES AND DYSLIPIDEMIA

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Objective:
Protein tyrosine phosphatase 1B (PTP1B) is a major negative regulator of insulin and leptin signaling. A novel biphenyl PTP1B inhibitor (VMNS2e) was synthesized in our laboratory which showed interactions with active site of PTP1B by docking and molecular dynamics. Effect of VMNS2e treatment on diabetes, insulin resistance and dyslipidemia was studied in obese (ob/ob) mice.

Materials and methods:
Blood glucose (BG) was measured after acute oral administration of VMNS2e (30 mg/kg) in both lean and ob/ob mice. In chronic study, VMNS2e (30 mg/kg) was given orally for 60 days and Metformin (300 mg/kg) was taken as standard therapy. Body weight, food intake, BG was measured weekly while glycosylated hemoglobin A_{1c} (HbA_{1c}), insulin, triglyceride, total cholesterol, low density lipoprotein (LDL), fructosamine, non esterified fatty acid (NEFA), liver and epididymal fat weight were estimated after the completion of study alongwith oral glucose tolerance test.

Results:
Acute dose of VMNS2e elicited an anti hyperglycemic effect by reducing BG by 14% (0.5 h) and 35.6% (6 h). Chronic VMNS2e treatment improved glucose tolerance by 25.3% and decreased BG levels. Hyperinsulinemia was reduced (19.6%). VMNS2e did not affect food consumption and body weight but it exhibited significant reduction (28.2%) in HbA_{1c}, plasma triglyceride (49%), LDL (24%) and fructosamine (13%) levels. It did not alter total cholesterol and NEFA levels. It reduced (26.3%) relative epididymal weight.

Conclusion:
VMNS2e exhibited acute and chronic anti hyperglycemic activity. It showed insulin sensitivity alongwith improvement in various lipid parameters and glycemic control which may be due to PTP1B inhibition.

Key words:
VMNS2e; PTP1B inhibitor; Diabetes; Insulin Resistance; Cardiovascular; ob/ob mice

INSULIN RESISTANCE IN NON-DIABETIC PATIENTS AT RISK FOR COGNITIVE IMPAIRMENT

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Abstract
Background:
Type 2 diabetes mellitus (DM) is associated with cognitive impairment. Peripheral insulin resistance is known to be the major contributor to the progression to hyperglycemia and DM. However, the relationship between insulin resistance and the risk of cognitive decline in non-diabetic patients is unclear.

Methods:
We analyzed 18 Alzheimer disease (AD) patients, 19 mild cognitive impairment (MCI) patients and 24 cognitively healty controls without diatetes. We examined demographic characteristics, current and past illness history and Mini-Mental State Exmination (MMSE). We also examined insulin resistance index (Homeostasis Model Assessment of Insulin Resistance, HOMA-IR) for indicator of insulin resistance and analyzed associated with cognitive decline.

Results:
Levels of HOMA-IR were significantly different among the 3 groups ($P<0.05$), and the highest HOMA-IR were detected in the AD group than MCI and controls groups. HOMA-IR levels are negatively correlated with MMSE ($p<0.01$) and among cognitive decline subjects, HOMA-IR levels were significantly correlated ($r=-0.351$, $p<0.01$). Multiple regressin analysis revealed that the level of HOMA-IR was independently asociated with cognitive decline ($p=0.04$).

Conclusions:
The HOMA-IR levels were associated with cognitive decline, and these results suggest that HOMA-IR may be an important risk factor on dementia.

METFORMIN, INSULIN RESISTANCE AND ITS EFFECT ON MORTALITY IN PATIENTS WITH CONGESTIVE HEART FAILURE

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Abstract
Background:
Patients with congestive heart failure (HF) have more insulin resistance as compared to the general population. Lower insulin sensitivity has been correlated with a decreased exercise tolerance as well as higher mortality rates in patients with HF. Previous published literature has shown metformin to improve insulin

resistance and lipid profiles in patients. We hypothesized that metformin treated patients with HF will have lower insulin resistance and subsequent mortality rates as compared to other patients.

Methods:
From Jan 2002 to December 2003, patients diagnosed with HF and diabetes mellitus (DM) at a single tertiary teaching institution were included in this study. Clinical, demographic, and mortality data were collected for these patients. Mortality data was assessed using the Social Security Master Deathfile.

Results:
Three hundred twenty seven patients (56.3% men and 69.5% Caucasians) with diabetes and HF comprised the study group. Out of these 327 patients, 185 patients died on follow up(mean ± SD: 1940 ± 203 days Range: 1590-2289 days). There were 37 patients who were on metformin. On univariate analysis, age ≥ 65 years, BMI < 30kg/m2, hemoglobin < 10gms/dl, creatinine ≥ 1.5 mg/dl and absence of statin or metformin use were associated with a higher mortality rate in patients with HF (Table 1). On multivariate analysis, age ≥ 65 years, BMI < 30kg/m2, hemoglobin < 10gms/dl and the absence of metformin were associated with mortality.

Conclusions:
Low BMI, increased age, anemia and lack of metformin use were all associated with increased mortality in HF patients with DM.

ACTIVE CORONARY PLAQUE IS ASSOCIATED WITH MULTI ORGAN INFLAMMATION

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Background:
We evaluated whether the coronary plaque with active inflammation could be associated with the systemic inflammation.

Methods:
Using whole body PET/CT, we observed total 90 subjects consisted of acute myocardial infarction (AMI) patients (n=32, 5712 years), chronic stable angina (CSA) patients (n=33, 6112 years), and controls (n=25, 578 years). Maximal standard uptake value (SUV) of the highest regions of interest was calculated in the right carotid artery, subcutaneous and visceral fat.

Results:
The SUV of AMI patients in the carotid artery and visceral fat was significantly higher than CSA patients or controls (AMI vs. CSA vs. controls; carotid artery: 2.880.43 vs. 1.780.43 vs. 1.670.27, respectively, p<0.05)

Conclusion:
These findings suggest that the inflammation of multiple organs such as visceral fat and carotid artery is associated with and may contribute to coronary plaque instability.

THE BENEFIT OF PRIMARY CARE PREVENTIVE INTERVENTION IN PATIENTS WITH METABOLIC SYNDROME

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Metabolic syndrome (MS) is related to cardiovascular risk factors that appear to promote the development of atherosclerotic cardiovascular disease and insulin resistance. Preventive measures are the main intervention in order to improve risk factors profile in MS patients.

The study is aiming to demonstrate the benefit of an intensive prevention programme conducted by general practitioners (GP), in patients with metabolic syndrome.

Materials and methods:
We conduct a prospective study of 18 months on 133 patients (mean age 55.6±8.3 years old, 65% women) previously diagnosed with MS based on NCEP-ATPIII criteria. The patients were evaluated by their GP at inclusion, followed by another 3 similar evaluation at 6 months. Each evaluation consisted in clinical examination and current laboratory blood tests. The GP's were reinforced to follow the current guidelines recommendations for lifestyle changes, cardiovascular risk factors control and drug prescription.

Results:
Using the paired t test to compare the data at baseline and after 18 months, we noticed significant improvement of the cardiometabolic risk factors: Waist circumference decreased with 2.5 cm, P=0.002; Systolic blood pressure decreased with 12 mmHg and diastolic blood pressure with 9 mmHg, P<0.001; Total cholesterol decreased with 15 mg/dL, P=0.006 along with LDL-cholesterol with 12 mg/dL, p<0.001; Fasting glucose decreased with 7.9 mg/dL, P=0.051 (ns). The improvement in HDL cholesterol and Triglycerides was not statisticaly significant.

Conclusions:
Eighteen months primary prevention programmes improves cardiovascular risk factors in patients with MS. Prevention programmes conducted by GP's are efficient, especially if the doctors are reinforced to follow the guidelines recommendations.

Acknowledgement:
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SLIDING-SCALE INSULIN (SSI) THERAPY- A SURVEY IN AN INNER CITY HOSPITAL

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Background:
In patient with diabetes, glucose control is often a difficult task. Traditional SSI regimens often ineffectively control glucose levels as they are unable to mimic physiologic insulin secretion. Despite expert opinions about doubtful efficacy and lack of evidence, it continues to be used in many hospitals across the US.

Methods:
A total of one hundred participants (53 residents and 47 nurses) were surveyed in a teaching hospital in an inner urban city. The respondents were asked to fill the survey confidentially.

Results:
Sixty-seven percent (67%) of total respondents viewed SSI as a bridging therapy; however a significant number (28%) were of the opinion that it is for treatment (15% residents and 50% nurses). Sixty-eight percent (68%) responders were comfortable administering SSI therapy. Ninety-eight percent (98%) agreed that glycemic control was erratic and eighty-eight (88%) encountered hypoglycemia at some point in patients on SSI. Seventy-nine (79%) never prescribed SSI as a sole therapy for good diabetic control. Majority (52%) felt that SSI is good for early and fast glucose control and 11% feared DKA if sliding scale was not prescribed. Before this survey only 53% of health care providers had searched literature and read about SSI. Sixty-six (66%) were of the view that American Diabetes Association (ADA) endorses SSI and 91% were of the opinion that this survey will help them in reading about SSI and using it appropriately in diabetic patients for good glucose control.

Conclusions:
The study concluded that the health care workers have strong and firm belief that SSI is endorsed by ADA and is useful for glucose control inspite of erratic blood sugar control and witnessed hypoglycemia. More education and awareness is needed to discourage this un-necessary use of sliding scale therapy in the hospital practice.

Key Words:
Sliding-scale insulin, Diabetes, Teaching hospital

Abbreviations:
SSI: Sliding-scale insulin, ADA: American Diabetes Association

PATHOLOGICAL TYPES OF FOSTERAGE AS A PROGNOSTIC FACTOR FOR CHILDRENS OVERWEIGHT

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Background:
We aimed to examine the relationship between a children's weight and family/psychosocial factors, to establish gender differences in eating behavior in obese children.

Methods:
This cross-sectional study involved 65 obese children (m / f = 33/32, mean age 13.5 ± 0.5 years) and 65 mothers. Psychological examination was conducted by Eidemiller test of family education and IEG-Kind test. All the analyses were performed with the Statistics 6.0 software, ANOVA test.

Results:
Significant gender differences ($p < 0.05$) were observed on the criteria: food remedy against the emotional stress, food as a problem; food restriction, fear of weight gain. In the girl's group were revealed a correlation with BMI: influence of foods ($r = –0.41$); forcing parents ($r = –0.45$). In puberty age girls observed a correlation BMI and points of IEG-Kind: food as a remedy against stress ($r = 0.41$); strength and the need for food ($r = 0.38$); dissatisfaction with their figures ($r = 0.45$), coercion by parents ($r = –0.78$). Two tests correlation analysis found differences depending on the stage of pubertat stage: in early puberty marked by a strong relationship between parents and the child's body weight ($r = 0.53$), increased fear of its increasing ($r = 0.56$).

Conclusions:
Findings indicated on the sex and age differences regarding its own body, restriction of food in children with obesity.

DURATION OF TYPE 2 DIABETES ILLNESS INFLUENCE ON THE GLYCEMIC CONTROL EFFECT OF CYCLOSET, A QUICK RELEASE FORMULATION OF BROMOCRIPTINE

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Brigham and Women's Hospital and Harvard Medical School, Boston, MA.

Cycloset is a quick release formulation of bromocriptine mesylate (bromo-QR), a centrally acting dopamine D2 receptor agonist indicated for the treatment of type 2 diabetes (T2DM). This novel once daily morning therapy improves glycemic control by lowering fasting as well as post meal glucose throughout the day without raising insulin levels by improving the body's responsiveness to insulin.

Methods:
A subset of the overall ITT study population from the Cycloset Safety Trial was established for those subjects with a baseline HbA1c of ≥7.5; taking one or two oral anti-diabetes drugs (OAD); with a week 24 HbA1c follow up measure; and who were ≥127 days drug compliant. Changes in HbA1c were assessed using linear regression models adjusted for various covariates and stratified by duration of illness.

Results:
We identified 379 qualified subjects with a mean HbA1c of 8.3% and mean age 58 yrs. The between group difference in HbA1c, adjusting for only baseline HbA1c was -0.60 ($P<0.05$) in favor of bromo-QR and -0.62 ($P<0.05$) in the fully adjusted model. The mean duration of T2DM was 8.1 years (tertiles defined as < 4.74, 4.74-8.56, and >8.56 years). For each tertile, differences in HbA1c were -0.86, -0.66 and -0.53, respectively.

Conclusions:
These findings suggest that bromo-QR as add-on to OAD therapy may be most effective when introduced early in the disease state. Additional studies are warranted to reaffirm these initial findings and to determine the contribution of bromo-QR effects on long term maintenance of ideal glycemic control.

THE PREVALENCE OF BROWN FAT AT THE METHODIST HOSPITAL IN HOUSTON, TX IS NOT AFFECTED BY THE SEASON

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Houston is one of the fattest cities in our country. Brown adipose tissue (BAT) is known to play a role in regulation of body weight in humans but until recently was thought to not be present in adults. The use of PET/CT scans has led to the identification of metabolically active brown adipose tissue (BAT) in US adults. We examined the prevalence of BAT in Houston. We hypothesized that we would find a high prevalence of BAT in Houston's multiethnic community as many of the groups represented here do have Asian ancestry. The role of seasonal variability in BAT activity suggested that Houston could have a lower prevalence than northern cities but we postulated that the intense air conditioning employed in the summer could actually provide a reversal of the seasonal influence seen in northern climates. We reviewed consecutive reports of positron emission tomography (PET) combined with x-ray computed tomography (CT) completed at The Methodist Hospital in 2007-2010. The overall prevalence rate of BAT was 2.37% with a similar prevalence among males and females. For race, the prevalence was greatest among Asians, followed by Mexican-Americans, then African Americans and Caucasians. We did not see a change in prevalence of BAT across calendar month. Our prevalence of BAT is much lower than the 7.3% prevalence reported by Cypess et al from the Beth Israel Deaconess Medical Center in Boston. Our finding of higher BAT detection rates in Asians and MAs suggests that genetics may be an important determinant of BAT prevalence.

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Background:
Several cross-sectional studies have shown the association between hyperglycemia and low levels of 25-OH-vitamin D (25-OHD<30 ng/mL). We previously found that adults with low 25-OHD were more like to have fasting hyperglycemia than those with sufficient 25-OHD. Data on the prospective risk for hyperglycemia and diabetes are less clear.

Methods:
We evaluated prospectively the association between 25-OHD levels (measured in 2000) and the risk of diabetes over a 10-year period in 68 normoglycemic adults (60% female with a BMI of 29.6 Kg/m²) recruited in a pilot study from an internal medicine clinic.

Results:
Subjects with low 25-OHD (20.3±5.1 ng/mL, n=58) were older than those with normal 25-OHD (33.2±3.2 ng/mL, n=10) (56.3 ± 10.9 yrs vs. 48.4±15.7 yrs). Diabetes developed in 24.1% of those with low 25-OHD and in 10% of those with normal 25-OHD (p=0.3). Fasting plasma glucose (117.9±51 mg/dL vs. 88.8±10.8 mg/dL, p=0.15) and hemoglobin A1c (7.6±2.1% vs. 6.2±0.6%, p=0.13) were observed for the low and normal 25-OHD groups, respectively.

Conclusion:
After 10 years of follow up, fasting plasma glucose, hemoglobin A1c, and incidence of diabetes were higher in the group with low 25-OHD levels, but these differences were not statistically

significant, likely due to the small sample size in the group with normal levels. Further studies with a larger sample size are warranted to assess the prospective risk for development of diabetes in those with low levels of 25-OHD, accompanied by studies assessing the potential benefits of vitamin D supplementation in those at higher risk for diabetes.

Authors are encouraged to include a brief clarification of the relationship of their topic to insulin resistance and/or to the above metabolic processes

There is accumulating evidence to suggest that altered vitamin D homeostasis may play a role in the development of impaired glucose metabolism and insulin resistance, hence leading to diabetes.

Our original study in 2000 showed a striking 40% prevalence of hypovitaminosis D in South Florida adult population.

The current hypothesis was that subjects who had hypovitaminosis D in 2000 have higher risk of developing diabetes ten years later compared to those with normal vitamin D concentrations at baseline.

In spite of the absence of a statistically significant difference, and acknowledging the limitation from a small sample size in the group with normal vitamin D levels, our results provide further insight to the relationship between vitamin D and insulin resistance and diabetes, and conveys the message to pursue further research to confirm if low vitamin D levels may be an independent risk factor for the development of diabetes, as well as to consider vitamin D supplementation as a potential intervention to decrease insulin resistance, especially for those at higher risk to develop diabetes.

INFLUENCE OF DIABETES MELLITUS ON THE PERIVASCULAR ADIPOSE TISSUE (PVAT) MODULATION OF AORTIC RINGS CONTRACTIONS

Enrique Hong[1] and Omar Echeverría[1]

PVAT modulates vascular smooth muscle contraction induced by several agonists; this effect is endothelial dependent and due to release of a substance. Therefore, it was decided to observe if such mechanism was also present in diabetic animals. Rats were treated with either 60 mg/kg of streptozotocin for type 1 diabetes (T1D), or with 65 mg/kg of streptozotocin plus 230 mg/kg of nicotinamide for type 2 diabetes (T2D) and rats were sacrificed 10 or 20 weeks after T1D or T2D, respectively. The aorta was removed and aortic rings with and without PVAT were placed in isolated tissue baths. Rings of control rats with PVAT produced smaller responses to norepinephrine, phenylephrine and 5-HT, than rings without PVAT. Incubation of rings with captopril or losartan increases the modulatory effects of PVAT. Rings from rats with T2D showed a modulation of the contractile responses to norepinephrine, phenylephrine and 5-HT, but such effect was smaller than in controls. However, rings from T1D rats showed an increase of the contractile responses to 5-HT, phenylephrine and norepinephrine in rings with PVAT. Therefore, the RAS seems to be involved in these effects, since both captopril and losartan increase the modulatory effect of PVAT on the vasocontractil responses to various agonists while RAS is present in adipose tissue. Partially supported by CONACYT 14473 and ICTDF PICSD0824.

Key Words:
Periarterial Adipose Tissue (PVAT); contraction modulation by PVAT; Diabetes Mellitus; Losartan; Captopril.

EFFECT OF *ENICOSTEMMA LITTORALE* BLUME EXTRACT ON BLOOD PRESSURE AND METABOLIC ALTERATIONS IN FRUCTOSE-INDUCED INSULIN RESISTANCE IN RATS.

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(My registration code is IRS1313)

Abstract

High fructose (HF) feeding induces a moderate increase in blood pressure in rats, which is associated with insulin resistance, hyperinsulinemia, and hypertriglyceridemia. The purpose of the present study was to investigate the preventive effect of *Enicostemma littorale* extract on hypertension, insulin resistance and its associated cardiovascular complications in HF fed rats. Rats were divided into four groups 1) Lab chaw fed rats 2) HF (70%) fed rats 3) HF + EL (2.5gm/kg/day) treatment 4) HF + Rosiglitazone (10mg/kg/day) treatment. EL and Rg treatment were given simultaneously with HF diet for 45 days. Untreated HF fed rats showed altered oral glucose tolerance, increased fasting insulin, fasting glucose level. They also exhibited hypertriglyceridemia, moderate level of hypertension, oxidative stress, platelet hyperaggregability, decreased prothrobin time and activated partial thromboplastin time, altered vascular reactivity and increased serum levels of enzymes CK-MB, SGOT, LDH and SGPT. HF fed rats treated with EL showed improvement in insulin resistance. They also showed reduced hypertriglyceridemia, oxidative stress, hypertension, platelet aggregability, blood coagulation, vascular reactivity, serum levels of marker enzymes for cardiac and hepatic functions. This effect of EL may be associated with the suppression of serum insulin, plasma triglyceride level, along with its antioxidant, anti-atherogenic and anti-thrombogenic potential in HF-induced hypertensive rats. In conclusion, our data indicate the preventive role of EL against fructose-induced insulin resistance and associated cardiovascular complications; hence this plant could be used as an adjuvant therapy for the prevention and/or management of chronic diseases characterized by hyperinsulinemia, hypertriglyceridemia, insulin resistance and aggravated antioxidant status.