ABSTRACTS
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FREE FATTY ACIDS (FFAS) - INDUCED INSULIN RESISTANCE MECHANISMS: CLINICAL INTERVENTION VERSUS TREATMENT FOR METABOLIC SYNDROME AND TYPE II DIABETES

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Abstract:
Increased fatty acid flux has been suggested to be strongly associated with insulin resistant states such as obesity and type 2-diabetes. We briefly have intended to summarize the major role played by FFA in insulin resistance induction. In muscle model, we have demonstrated that both oleate and palmitate treatment were able to increase the serine 307 phosphorylation for IRS-1 due to the PKC activation. IRS-1 Serine307 phosphorylation is inducible which causes the inhibition of IRS-1 tyrosine phosphorylation by either IκB-kinase (IKK) or c-jun N-terminal kinase (JNK). Furthermore, our data have also manifested that the two FFAs activate the IKKα/β, the stress kinases S6 kinase p70 (p70SK), stress-activated protein kinase (SAPK), JNK, and p38 MAP kinase (p38MAPK).

In liver model, FFA flux may cause perturbations in the hepatic insulin-signaling cascade through protein kinase C (PKC) activation following fructose feeding in the hamster model. This effect was reversed by bisindolylmaleimide-I, (Bis-I). We further assessed the effect of PKC inhibition on lipid metabolism, apolipoprotein B (Apo B100). The current data point out the link between enhanced FFA flux and activation of PKC and how it impacts on both the insulin signaling as well as lipid metabolism in muscle and liver.

At the diagnostic level, the magnitude and composition of inflammatory cytokine response as well as other mediators in the circulation of pre-diabetic patients may provide an important insight. As a result, the robustness for measuring and screening for type II diabetes as a diagnostic tool for predicting insulin resistance and metabolic syndrome is considered an important clinical intervention.

Key words:
Free fatty acid (FFA); Insulin Resistance; Skeletal Muscle Cell, C2C12; Protein Kinase C (PKC), Insulin Receptor Substrate protein-1 (IRS-1), Clinical Biochemistry, Molecular Endocrinology and type 2 Diabetes.

PREVALENCE OF INSULIN RESISTANCE SYNDROME IN ADULTS FROM 8 DISTRICTS IN SOUTHINDIA ACCORDING TO ATP III DEFINITION

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Background and Aim:
In 2001, the Third Report of the National Cholesterol Education Program Adult Treatment Panel (ATP III) proposed a new definition for insulin resistance syndrome (IRS). The aim of this study was to estimate the prevalence of IRS in several districts in south india using ATP III criteria.

Material and Methods:
All studies of IRS prevalence in subjects 18 years of age or older, defined by ATP III, were included. Search was done up to August 2003 in Internet database. Studies in special populations (offspring from diabetics, workers with high physical activity, athletes), and further studies with the same population were excluded (the study with the greater population was chosen). Studies in populations with extreme age ranges were also excluded. Finally, studies from 8 districts were analysed: Anantapur,Kadapa,Chittor,Vijayawada,Ongole,Khamam,Kurnool,and Nellore.

Results:
Data of 5492 subjects were collected. The prevalence of IRS was variable (12.7% - 38.7%). Overall prevalence was 21.3% (CI 95%: 14.9 - 27.7; n=66398). The distribution by sex was very similar (20.3% [CI: 13.8 - 26.9] and 22.4% [CI: 15.2 - 29.6] in men and in women, respectively; $p>0.05$

Conclusions:
The prevalence of insulin resistance syndrome in the 8 districts studied was high and variable by ATP III definition. It is important to determine the global prevalence of this syndrome because it is a major problem of public health.

RELATIONSHIP OF INSULIN RESISTANCE WITH ANTHROPOMETRIC INDICES OF OBESITY IN IMPAIRED GLUCOSE TOLERANT AND TYPE 2 DIABETIC PAKISTANI SUBJECTS

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Back ground:
Insulin resistance and obesity are particularly important not only in the pathophysiology of diabetes mellitus but also a major CVD risk factor, independent of hyperglycemia.

Objective:
This study was aimed at determining the correlations among anthropometric indices of obesity (waist circumference, WHR & BMI) and insulin resistance in impaired glucose tolerant and type2 diabetic subjects.

Methods:
A total number of 400 subjects (204 males and 196 females) of age between 45-65 years were included in the study. Oral glucose tolerant test was employed to confirm the glycemic status on the first visit of the patients in the hospital. Anthropometric and biochemical characteristics of study population including age, BMI, were recorded. Fasting plasma glucose and HbA1c were measured by glucose oxidase and low pressure cation exchange chromatography. Serum fasting insulin was assessed by ELISA. Homeostasis model of assessment was employed to assess the level of insulin resistance.

Results:
Following the WHO cutoffs for Asians, 35% of our sample population was found to be overweight and 65% were obese, 67% had WHR greater than 1. BMI was greater in females while WHR values were higher in males. A significant association was found between insulin resistance and WHR in pre-diabetic subjects ($r = -0.368$, $p<0.05$). A positive significant correlation of insulin resistance was found with WHR ($r= 0.31$) and BMI ($r= 0.47$) in type 2 diabetic subjects, while WHRwas determinant in IGT subjects ($r =0.541$).

Key words:
BMI, WHR, Insulin resistance.

THE INFLUENCE OF METABOLIC SYNDROME AND GLUCOSE TOLERANCE ON THE INCRETIN EFFECT

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Background and aims:
Metabolic syndrome (MS) and impaired glucose tolerance (IGT) are high risk conditions for type 2 diabetes, a disease where the incretin plasma levels or biological activity have been shown to be reduced. Previous data indicate that normotolerant (NGT) subjects with the MS have an increased early phase insulin secretion during OGTT, as measured by insulinogenic index (IG30), in comparison to individuals without the metabolic syndrome, independently from insulin resistance. The present study was undertaken to further investigate the alpha and beta cell function and entero-insular axis in these pre-diabetic conditions.

Materials and Methods:
Using oral (OGTT) and intravenous (IVGTT) glucose tolerance test we studied alpha and beta cell function, insulin resistance, incretin levels and their relationship to impaired glucose tolerance state in 139 subjects with normal fasting glucose, with (59) and without MS (80).

Results:
Among normotolerant subjects, MS+ individuals showed in comparison with MS-: higher AUC (0-10) for glucose ($p<0.05$) but similar first phase insulin secretion (p=ns) as measured by ΔAIR_G and AUC (0-10) for insulin during the IVGTT; increased (p=0.04) AUC (0-60) for insulin during the IVGTT, although this difference disappeared when HOMA-IR was used as covariate; similar AUC (0-120) for GLP-1 and GIP (p=ns) during the OGTT; higher glucagon suppression relative to the increase of glucose (p=0.002) but similar glucagon levels (p=ns). Among impaired glucose tolerance subjects, MS+ individuals showed no statistically significant differences in the above parameters. When taken together IGT subjects showed in comparison to NGT individuals: decreased ΔAIR_G ($p<0.01$) and AUC (0-10) for insulin during IVGTT, and these differences remained when HOMA-IR was used as covariate; similar (p=ns) AUC (0-60) for insulin during the IVGTT; higher GIP plasma levels and AUC (0-120) for GIP ($p<0.05$) during the OGTT; similar (p=ns) AUC (0-120) for GLP-1 and glucagon levels; lower glucagon suppression relative to the increase of glucose (p=0.04).

Conclusion:
In contrast to the data obtained with OGTT, NGT subjects with metabolic syndrome did not show at the IVGTT an

increase of early phase insulin secretion. This difference might be due to an increased incretin effect as suggested also by the higher glucagon suppression in relation to the increase of glucose observed in these subjects. IGT subjects try to compensate the impaired beta-cell secretory capacity by an hyper activation of incretin axis as suggested by the increased GIP levels but they fail to restore an adequate insulin secretion and glucagon suppression relative to the glucose rise. Alike we observed the failure of these compensatory mechanisms when the two defects, metabolic syndrome and impaired glucose tolerance, are associated.

PREVALENCE OF CANCER AND OBESITY IN UNDERGOING EPIDEMIOLOGICAL TRANSITION COUNTRIES: A CROSS-SECTIONAL POPULATION-BASED SURVEY IN MEXICO

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Background:
The prevalence of both overweight and obesity in adults and children has been increasing. Moreover obesity has been associated with breast cancer and other cancers located in the colon, endometrium, kidney, esophagus, and stomach. Our purpose was to assess the prevalence of cancer in subjects with obesity.

Methods:
The trained field staff of National Institute of Health Public from Mexico conducted a cross-sectional population-based survey using a questionnaire and simple measurements of body mass index (BMI), waist circumference, and blood pressure. All subjects of the population cohort greater that or equal to 20 years were included to analysis.

Results:
A total of 33,035 subjects of both gender were included, 23,674 patients with obesity and overweight, and 9,361 normal subjects according to the World Health Organization criteria. Mean age of both sexes was 43 ± 16 years. In women the prevalence of abdominal obesity was significantly ($p<0.0000001$) higher (85.6%, 95% CI, 85-86) compared that males (65.3%, 95% CI, 65-66). The prevalence of stomach cancer was high in females with overweight, and in males with normal BMI. Furthermore, in women the prevalence of melanoma and cervical cancer increases with increasing BMI. Similar data was observed in males with prostate cancer (Table 1). The lowest prevalence of cancer was leukemia in both genders.

Conclusions:
These data indicate that in countries undergoing epidemiological transition the implementation of program for prevention and detection of non-communicable chronic diseases (NCCD) is essential to prevent the increasing of their prevalence and therefore, decrease the prevalence of cancer related to NCCD.

Table 1
Prevalence of cancer according to Body Mass Index criteria from World Health Organization by gender, and per 100,000 populations

	Females.				Males.			
Cancer type.	Normal n=5253	Overweight n=7497	Obesity n=7243	Total N=19993	Normal n=4108	Overweight n=5737	Obesity n=3197	Total N=13042
Cervical Cancer	513.99	693.61	731.74	660.23				
Prostate Cancer					73.03	87.15	125.12	92.01
Breast Cancer	209.40	320.13	220.90	255.09	0.00	34.86	0.00	15.34
Melanoma	19.04	26.68	27.61	25.01	24.34	52.29	31.28	38.34
Stomach Cancer	19.04	53.35	0.00	25.01	48.69	17.43	0.00	23.00
Leukemia	0.00	13.34	0.00	5.00	24.34	0.00	0.00	7.67

SERUM RETINOL BINDING PROTEIN IN PATHOGENESIS OF TYPE 2 DIABETES MELLITUS IN HUMANS

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Background and aims:
Serum retinol binding protein 4 (RBP 4) has been found to be significantly enhanced in type 2 diabetes mellitus (DM), hence, might be playing a role in the pathogenesis of type 2 DM.

Materials and methods:
Serum protein profile of type 2 diabetic patients and normal glucose tolerance (NGT) subjects was resolved by two dimensional gel electrophoresis using Bio-Rad Protean IEF strip method. RBP 4 was identified and quantified by MALDI-TOF and Gene Genius Bio-imaging gel documentation system. Fasting blood glucose, fasting insulin and glycated hemoglobin (HbA1C) were measured by enzyme linked immunosorbent assay (ELISA) and automated clinical chemistry analyzer. Insulin sensitivity was determined by homeostatic model assessment insulin resistance index (HOMA-IR). Body mass index (BMI) and waist to hip ratio (WHR) were also evaluated to study their correlation with RBP 4.

Results:
Fasting serum RBP 4 levels were found to be significantly and positively correlated (P<0.01) with HOMA-IR in type 2 diabetics. A positive correlation was also observed when fasting serum RBP 4 levels were compared with fasting insulin (P<0.05), BMI (P<0.001), and WHR (P<0.01). Further, BMI, as revealed by multiple linear regression model, was found to be a significant determinant of serum RBP 4.

Conclusion:
A positive correlation of serum RBP 4 with insulin resistance, in type 2 diabetics, and also with fasting insulin, BMI and WHR suggests its possible role in the pathogenesis of type 2 diabetes mellitus in human.

INSULIN RESISTANCE IS SIGNIFICANTLY ASSOCIATED WITH SERUM BILIRUBIN LEVELS IN IN IMPAIRED GLUCOSE TOLERANT PAKISTANI SUBJECTS

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The protective role of serum bilirubin due to its antioxidant activity against insulin resistance has been suggested. Present study aims to determine the relationship of serum bilirubin with the other biochemical parameters of insulin resistance. In this cross sectional study a total of 200 impaired glucose tolerant subjects visiting an outpatient clinic, were selected by OGTT. The anthropometric characteristics included age, sex, weight, height, waist hip ratio and family history. Biochemical parameters included fasting glucose level, HbA1c, lipid profile, ALT, AST, alkaline phosphatase, and bilirubin levels which were assessed by routine chemistry analyzer. Serum insulin was assessed by ELISA. Insulin resistance was calculated by (HOMA- IR). All analysis was performed using SPSS software (SPSS version 13.0, Chicago, IL, USA). All serum samples were collected after 12 hours of fasting. Liver enzymes were present in normal reference range. There was a significant low level of bilirubin, high level of triglycerides and low level of HDL (P<0.01) in the study population. Marked hyperinsulinemia and insulin resistance was observed among IGT subjects. Glucose and HbA1C levels had a significant positive correlation with BMI and waist hip ratio (p<0.01). Serum bilirubin level was significantly correlated with high triglycerides (r=-0.363 and P<0.001). There was a significant correlation present between serum bilirubin and HDL levels(r=0.497 and p<0.001). Significant inverse relationship was present between insulin resistance and bilirubin levels(r=-0.372, p<0.001).

Conclusion:
Serum bilirubin level is significantly associated with potential risk factors of diabetes and insulin resistance.

Key Words:
Bilirubin, insulin resistance, triglycerides, HDL, IGT.

INSULIN-LIKE EFFECTS OF C-PEPTIDE IN ADIPOSE TISSUE OF DIABETIC RAT

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Objective:
New data indicate that connecting peptide (C-peptide) exerts insulinomemitic actions in different tissues. In this study, we tested the hypothesis that C-peptide exerts insulin-like effects in adipose tissue.

Methods:
Two groups of streptozotocin-induced diabetic rats were used: insulin-treated diabetic group (ITD, n = 6) which received insulin (sc) from two days after induction of diabetes to day seven (date of surgery); non-treated diabetic group (NTD, n = 12) which received buffer. The animals were sacrificed and the retroperitoneal adipose tissue was excised, minced and subjected to *ex-vivo* organ culture for 24 hours. The tissue pieces were then preincubated (30 min) with vehicle, L-NAME or cilostamide (a phosphodiesterase-3B inhibitor) before treatments (90 min) with C-peptide, insulin, isoproternol, or a combination of them.

Results: I
n adipose tissue of ITD rats, C-peptide caused a significant decrease in basal lipolysis which was comparable to that found with insulin. The peptide had no overall effect on isoproterenol-stimulated lipolysis in this group. In the tissue of NTD rats, C-peptide like insulin failed to show any effect on the basal lipolysis. Also, the inhibitory effect of insulin on isoproterenol-stimulated lipolysis was mimicked by C-peptide. This antilipolytic effect of C-peptide was remained at presence of L-NAME but prevented by cilostamide.

Conclusions:
This is the first report demonstrating that C-peptide inhibits lipolysis in diabetes condition primarily via activation of phosphodiesterase-3B. The effect suggests the possibility of a clinically applicable role for C-peptide replacement, together with the classic insulin therapy, to mitigate fat mobilization in patient with type-1 diabetes.

Key worlds:
C-peptide, Diabetes, Lipolysis, Adipose tissue, Rat

EPIDEMIOLOGICAL SURVEY IN DIABETES MELLITUS AND ITS COMPLICATIONS IN SAVOJBOLAGH RURAL AREA

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Introduction:
Diabetes mellitus (DM) results from a lack (or diminished effectiveness) of endogenous insulin. Hyperglycemia is just one of a far-reaching metabolic derangement, which may cause serious microvascular (retinopathy, nephropathy, neuropathy) or macrovascular complications (cardiovascular-coronary artery disease, cerebrovascular-stroke, and peripheral vascular).

Prevalence of DM is about 3% worldwide and according to new lifestyle, it is predicted to grow over next years. In Iran, recent studies have shown not only about 5-6 % of 3 to 69 year old Tehraian have DM but also about half of them did not know their illness.

The main goal of this study was to illustrate the prevalence of diabetes mellitus and its complications in Savojbolagh in the west of Tehran province.

Material & methods:
19880 over 29 year old women and men were included in this cross-sectional study from January 2008 to July 2008 in Savojbolagh rural areas. Fasting blood sugar were measured in five age categories in both sexes as a criterion of hyperglycemia and DM in any over 29 years old person with obesity or over weight (BMI ≥ 25), positive past familial history of DM, clinical signs (at least two signs), blood pressure(BP)> 140/90, any sign of DM complications.

Base on the results of FBS, we had three groups in next step:

1. FBS≤110 mg/dl, High Risk Group
2. 110< FBS < 126 mg/dl, Prediabetic Group
3. FBS ≥ 126 mg/dl that repeated after two weeks.

The second FBS gave us three groups again. The first two groups were the same as the results of last FBS but the third group was considered as diabetes mellitus.

Previous known diabetic patients were separated and examined for diabetic complication by physicians at first step, and then they were included to total diabetic patinas (previous and new diabetic patinas).

Results:
The subjects were11783 (59.3%) female and 8097(40.7%) male. Prevalence of diabetes mellitus (DM) was 5.3% (previous and new diabetic patinas), prediabetics 2.7% and high risks 37.8% in general and more common in women in all the age categories. The most common complications were cardiovascular-coronary artery disease (8 cases) and cerebrovascular-stroke (6 cases).

Measuring blood pressure (BP) illustrated that elevated BP cases were seen more in over 70-year olds (26.6%) and 60 to 69-year olds (24.6%).

Consequences:
The prevalence of DM in Savojbolagh rural area is more than global prevalence; however it is almost equal to Tehran prevalence. In the selected area DM, Prediabetic conditions and High risk conditions in women are more common than men except over 70-year olds who newly diagnosed as diabetics. Different in the number of the women and the men in each clinical condition decreased by increasing the age. The number of elevated BP in both sexes rose by increasing age. To sum up, it seems effective health managing which gives people information about DM and its complications can change the view to life and modify behavior in lifestyle in order to reduce DM and its complications.

Key word :
FBS – BMI – blood pressure – DM – Savojbolagh – Iran University

EFFECTS OF INCREASED FASTING BLOOD SUGAR ON SERUM LEVEL OF TRIGLYCERIDE, CHOLESTEROL AND CREATININE

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Background and Aims:
Increased blood sugar exerts pathophysiological effects on blood biochemistry. The main aim of this study was to determine the effects of increased blood sugar on serum level of triglyceride, cholesterol and creatinine in patients with high fasting blood sugar.

Materials and Methods:
Blood samples of 100 male or female patients with higher fasting serum glucose (>180 mg/dl), and of 100 male or female subjects with normal fasting blood glucose (70-115 mg/dl) were biochemically analyzed for triglyceride, cholesterol or creatinine level. The normal subjects were correlated with patients concerning age, sex, diet and habitat. Serum levels of triglyceride, cholesterol or creatinine were compared statistically between the groups using Kruskal–Wallis one-way analysis of variance.

Results:
Increased blood sugar (>180 mg/dl) caused to significant increasing of serum triglyceride level (P=0.008), however, did not significantly influence serum level of cholesterol (P=0.524) or creatinine (P=0.962).

Conclusion:
Increased fasting blood sugar can raise serum level of triglyceride partly because of its effects on biochemical pathways involving in converting extra glucose to triglyceride.

Key words:
Fasting Blood Sugar, Triglyceride, Cholesterol, Creatinine.

EFFECTS OF TESTOSTERONE AND DIAZOXIDE ON SERUM INSULIN LEVEL IN MALE RATS

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Background and Aims:
Diazoxide is used clinically in the treatment of hyperinsulinism, insulinoma and hypoglycemia. This drug can suppress insulin release. Androgens also have effects on insulin secretion. The aim of this study was to determine the effects of co-administration of testosterone and diazoxide on serum insulin level in male rats.

Materials and Methods:
Diazoxide (30 mg/kg/day) was administered in drinking water. Testosterone enantate (10 mg/kg/day) was injected intraperiotenally. After 4 weeks, blood samples were collected and serum insulin was measured and compared statistically between the groups (ANOVA).

Results:
Diazoxide administration caused to decraesing of serum insulin level (P<0.01). However, testosterone administration resulted in increasing of serum insulin level (P<0.05). Co-administration of testosterone and diazoxide had the same effects as diazoxide.

Conclusion:
The results of our study show that testosterone can not prohibit the decraesing effects of diazoxide on insulin secretion in male rats.

Key words:
Insulin, Diazoxide, Testosterone

EFFECTS OF INCREASED FASTING BLOOD SUGAR ON SERUM LEVEL OF ALKALINE PHOSPHATASE, ALANINE AMINOTRANSFERASE AND ASPARTATE AMINOTRANSFERASE

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Background and Aims:
Increased blood sugar is a pivotal factor contributing to diabetes and exerts important effects on body biochemistry. The main aim of this study was to determine the effects of increased blood glucose on serum level of alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

Materials and Methods:
Blood samples of 200 male or female patients with high blood glucose level (100 patients with fasting glucose between 115 and 180 mg/dl, and 100 patients with fasting blood glucose higher than 180) and, of 100 male or female subjects with normal fasting blood glucose (70-115 mg/dl) were biochemically analyzed for alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase. The normal subjects were correlated with patients with respect to age, sex, diet and habitat. Serum levels of ALP, ALT or AST were compared statistically between the groups using Kruskal–Wallis one-way analysis of variance.

Results:
Increased blood sugar (higher than 115 mg/dl) resulted in increased serum level of ALP (P=0.022), however, did not significantly influence serum level of ALT (P=0.991) or AST (P=0.303).

Conclusion:
The results of our study show that increased fasting blood sugar can raise serum level of ALP partly because of its effects on cellular or tissue disturbances in our body.

Key words:
Fasting Blood Sugar, ALP, ALT, AST.

MACRONUTRIENT COMPOSITION IN WEIGHT LOSS DIETS – A META-ANALYSIS

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Background:
Despite their poor long term performance, dietary interventions for weight loss remain the first line treatment for obesity. In addition to energy restriction, some diets emphasize manipulation of macronutrient composition to promote weight loss. Such diets may be broadly classified into low fat and low carbohydrate diets.

Objectives:
This meta-analysis was designed to compare low fat to low carbohydrate diets in terms of weight loss or maintenance of weight loss.

Methods:
Studies were included in the present meta-analysis if they were 1) well-designed randomized clinical trials comparing low fat to low carbohydrate diets; 2) included healthy overweight and obese adults; 3) measured body weight as the primary endpoint; 4) were published in 2009 or later.

Results:
Four studies meeting all inclusion criteria were identified. Together, these studies 1878 subjects, 941 of whom were exposed to low carbohydrate diets and 937 to low fat diets. Two of the studies targeted weight loss as the primary endpoint, and two studies maintenance of weight lost using meal replacement products. Overall compliance was poor and attrition was high across studies. In a random effects model, no significant advantage to either diet strategy could be identified – standardized difference in means -0.07, 95% CI -0.3-0.4, p=0.7.

Conclusions:
Manipulation of macronutrient composition of weight loss diets does not appear to be associated with significantly different weight loss outcomes. Both types of macronutrient-centered weight loss diets appear to be associated with poor adherence and high attrition rates. Novel weight loss strategies must be investigated.

THE ANTI-OBESITY EFFECTS OF SEMEN CASSIAE RECIPE BY INCREASING MRNA EXPRESSIONS OF B3-AR AND UCP-2 IN ADIPOSE TISSUES OF DIET-INDUCED OBESE RATS

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Objective:
For the first time our study invented a new recipe: SC, which was composed of semen cassiae and turmeric. We researched anti-obesity effects of SC, and its influence on mRNA expressions of β3-AR and UCP-2 in adipose tissue.

Methods:
Fifty male SD rats were divided into control group (*n*=8) on ad libitum diet, and obese model group (*n*=42) on a diet of high fat chow for 2 weeks. Then 29 selected nutritional obese rats were divided into three groups: untreated obese model group (*n*=9); metformin group (*n*=10), orally given metformin; SC group (*n*=10), orally administrated SC, for 8 weeks respectively. Body weight, wet weight of visceral fat and PBF of rats were measured. The levels of serum fasting blood glucose, lipid and insulin were assessed and ISI was calculated. Changes of adipose tissue with Hematoxylin-Eosin stain were checked by light microscope, and cellular diameter and quantity of adipocytes were evaluated. Finally, mRNA expressions of β3-AR and UCP-2 from perirenal fat were detected by RT-PCR.

Results:
Compared with obese model group, body weight, wet weight of visceral fat and PBF in SC group decreased significantly (*P*<0.01), level of HDL-C increased markedly (*P*<0.01), ISI was higher (*P*<0.01), diameters of adipocytes diminished significantly (*P*<0.01), and mRNA expressions of β3-AR and UCP-2 from perirenal fat were greatly increased (*P*<0.05).

Conclusions:
SC could reduce body weight and adipocyte size through up-regulating mRNA expressions of β3-AR and UCP-2 in adipose tissue, and improving insulin sensitivity in diet-induced obese rats.

Abbreviations:
SC, *Semen cassiae* recipe; β3-AR, β3 adrenergic receptor; UCP-2, uncoupling protein 2; ISI, insulin sensitivity index; PBF, percentage of body fat; RT-PCR, reverse transcription polymerase chain reaction.

Keywords:
Semen cassiae recipe (SC); Obesity; Beta 3 adrenergic receptor (β3-AR); Uncoupling protein 2 (UCP-2); Diet-induced obese rats

THE EFFECTS AND ITS MECHANISMS OF ZHENQING RECIPE ON TGF-β1 IN DIABETIC NEPHROPATHY WITH HYPERTENSION RATS

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Objective:
To observe effects of Zhenqing Recipe (ZQR) on TGF-β_1 in diabetic nephropathy (DN) with hypertension rats and research its mechanisms.

Methods:
DN with hypertension models were made by 4 weeks high-salt diet with high sugar and fat for male Wistar rats, and intraperitoneal injection of streptozotocin. The model rats were randomly divided into three groups: untreated model group (n=15); metformin group (n=15), orally given metformin; ZQR group (n=15), orally administrated ZQR, for 8 weeks respectively. Blood pressure was measured before modeling and after treatment of 2, 4, 8 weeks. FBG, TG, TC and UAE of rats were observed and recorded. Renal histomorphology with PAS staining was observed by the light microscope. TGF-β_1 in kidney was detected by immunohistochemical assay, and TGF-β_1 mRNA in renal cortex was detected by RT-PCR.

Results:
Initial blood pressure of rats has no significant difference before modeling (*P*>0.05). After 4 weeks of treatment, compared with model group, blood pressure in metformin group decreased (*P*<0.01), blood pressure in ZQR group was slightly lower (*P*<0.05). When 8 weeks, rebound of blood pressure in metformin group is appropriate with the model, blood pressure of ZQR reduced significantly (*P*<0.01). Compared with model group, FBG, UAE and TG in ZQR group and metformin group significantly decreased

(P<0.01), TC levels also decreased (P<0.05). Level of TGF-β_1 in ZQR group and metformin group decreased (P<0.01), and level of TGF-β_1 in ZQR group was lower significantly than that in metformin group (P<0.05). TGF-β_1 mRNA expression in ZQR group and the metformin group were significantly lower than model group (P<0.01). Pathological changes were ameliorated in ZQR and metformin group compared with model group.

Conclusion:
ZQR can regulate blood pressure and improve renal functional morphology through down-regulation of TGF-β_1 and its mRNA expression in DN with hypertension rats. We initially proved that inhibition effect of TGF-β_1 in ZQR is better than metformin, and ZQR can lower blood pressure to normal level.

Key words:
Zhenqing Recipe (ZQR); hypertension; diabetic nephropathy (DN); transforming growth factor-β1 (TGF-β1)

Abbreviations:
ZQR, Zhenqing Recipe; DN, diabetic nephropathy; TGF-β_1, transforming growth factor-β_1; FBG, Fasting blood glucose; TG, triglyeride; TC, total cholesteral; UAE, urine albumin excretion; RT-PCR, reverse transcription polymerase chain reaction.

HIGH COMPLEX-CARBOHYDRATE DIET IMPROVES METABOLIC, INFLAMMATORY AND ANRTOPOMETRIC MARKERS IN HYPERINSULINEMIC INDIVIDUALS

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Aims:
To evaluate the effect of high complex-carbohydrate diet on weight reduction, metabolic and inflammatory profile in a group of apparently healthy individuals, as well as to establish the effect of the diet on hyper-insulinemic individuals.

Methods:
72 women and men (age 50±9 years, BMI 31.5±5.6 kg/m^2) were given high complex carbohydrate diet for 8 weeks. The diet composition was: 1200-1600 Kcal, 60-62% carbohydrates, 30% fats, 10% proteins.

Results:
The high complex carbohydrate diet significantly reduced BMI (31.5±5.6 vs. 30.2±5.5, p< 0.001), waist (101±16.7, vs. 96±16.3, p< 0.001) and hip (113±12.8, vs. 110±11, p< 0.001) circumferences, fasting triglycerides (130±61 vs. 114±44, p=0.001), total (224.5±38.7 vs. 199.5±30.2, p< 0.001) and LDL cholesterol (143.7±32.8 vs. 126.3±24.3, p< 0.001), as well as the inflammatory profile, including the ESR (22.5±14.5 vs. 17.9±11.5, p< 0.001), high sensitivity CRP (5.5±4.2 vs. 3.6±2.9, p< 0.001), fibrinogen (308.6±56.6 vs. 298.5±51.5, p=0.005), the white blood cell count (7.4±0.3 vs. 6.9±0.4, p< 0.001). ICAM levels were higher and decreased more significantly in hyperinsulinemics (258.5±13.4 vs. 233.2±12.4 p< 0.0001), compared to normoinsulinemics. Insulin decreased significantly only in hyperinsulinemics (30.4±1.5 vs. 21.9± 1.2 in women and 33.4±2.3 vs. 25.8±1.2 in men, p< 0.0001), with no changes in normoinsulinemics, as well as HOMA-R (7.0±0.5 vs. 5.0±0.3 in women and 8.8±1.0 vs.6.2±0.5 in men, p=0.03).

Conclusions:
A high complex-carbohydrate diet is effective in improving the individuals´ anthropometric measurements, metabolic and inflammatory markers in normo and hyperinsulinemic individuals.

IGF-1 WAS SIGNIFICANTLY LOW AMONG NEWLY DIAGNOSED TYPE 2 DIABETIC PAKISTANI SUBJECTS

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Diabetes mellitus refers to a range of conditions that are all characterized by elevation of the blood glucose level due to insulin deficiency or impaired insulin action. The aim of this study was to determine the level of insulin like growth factor-1 among type 2 diabetic mellitus (T2DM) patients in Pakistan. The IGF-1 is an important and preferred biomarker of diabetes. This study was done to evaluate the levels of IGF-1 (pg/ml) among T2DM patients with potential risk factors of diabetes including glycemic levels, BMI, WHR and lipid profile. Total 88 subjects were included in this study in which 29 subjects were male and 59 subjects were females with age range of 36-70 years. These subjects have higher BMI and were obese. The subjects were stratified into 3 categories on the basis of glycemic status. Serum IGF-1 level (pg/ml). and Insulin level were assessed by ELISA technique. In present study, all the diabetic patients have significantly lower levels of IGF-1 (p<0.05). It was concluded from present study that

there was a positive correlation between IGF-1 and insulin sensitivity (r=0.58,p<0.05) while an inverse correlation between IGF-1 levels and Glycemic status (r=0.746, p<0.05) was observed.

Key words:
IGF-1,Insulin sensitivity, WHR, Lipid profile.

SERUM VITAMIN D LEVEL IS SIGNIFICANTLY ASSOCIATED WITH INSULIN RESISTANCE AMONG TYPE 2 DIABETIC PAKISTANI SUBJECTS

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Abstract:
Pakistan is among one of the countries who has most rapidly growing number of people with Diabetes mellitus. The aim of the present study was to assess the Vitamin D status in T2DM subjects of Lahore in order to evaluate its relationship with associated potential risk factors. This cross sectional study was conducted on 90 Type 2 diabetic patients who attended Amin Hayat Diabetic Center in Lahore from Jan 2011 to June 2011. Patients with age 37 to 67 years included 29 males and 61 females. Three groups were made based on glycemic level .The demographic parameters including age, BMI, B.P, personal history, socioeconomic status were recorded. The biochemical parameters including FPG, RPG, and HbA1c and lipid profile were measured by chemistry analyser. Insulin and Vitamin D level were assessed by ELISA. Insulin resistance was calculated by HOMA-IR. Among these subjects significantly low level of vitamin D was observed. Vitamin D was significantly associated with HDL and HbA1c in the studied population. According to the present study there was significant (p<0.05) inverse correlation of glycemic level and insulin resistance with Serum Vitamin D level (r=0.63, r=0.72) respectively.

Key words:
Insulin resistance, lipid profile, Vitamin D, HbA1c

AMELIORATION OF SUCROSE INDUCED NON-ALCOHOLIC FATTY LIVER DISEASE THROUGH *TRIDAX PROCUMBENS*.L.IN RATS

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Introduction:
Non-alcoholic fatty liver disease (NAFLD) and its prevalence is only 2 - 3% in the general population. Obesity, diabetes, hyperlipidemia and female sex are important risk factors for NAFLD. Most patients are asymptomatic, have mild-to-moderate elevations of serum aminotransferase levels, noxious stimuli, including hypoxia, systemic inflammation, malignancies, deficiencies, starvation, and various metabolic derangements. Insulin resistance syndrome is the only metabolic syndrome that has been consistently associated with NAFLD. Accumulation of lipids in nonadipose tissues can lead to cell dysfunction and cell death, a phenomenon known as lipotoxicity. . NAFLD state is also characterized by an increase in proinflammotary cytokines such as tumor necrosis factor - α (TNF-α), which may also contribute to hepatocellular injury.

Purpose:
The NAFLD, the disease of civilization is threat to human health of current civilized society which needs immediate attention and management. *Tridax procumbens* is a proven previously in our lab antihyperinsulinimic, antilipidemic, hypoglycemic, hypotensive and hepatoproductive herb. Hence this study aims at the Amelioration of sucrose induced Non-alcoholic Fatty liver disease through *Tridax procumbens*. L.in rats.

Material:
In the male albino Wistar rats (95 to 110 gm) NAFLD 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. In liver weight, protein, lipids, glycogen, antioxidant enzyme and thiobarbituric acid reactive substance (TBARS) were estimated.

Results:
The livers of sucrose fed rats (Group 2 and 8) are brighter than all other groups. Bright liver may me be the marker for non-alcoholic fatty liver disease. The elevated liver weight, total lipids, liver triglycerides TBARS and elevated serum AST, ALT, GGT and decreased liver protein, glycogen, antioxidant enzymes of liver were observed in sucrose fed animals. The above changes were ameliorated when fed with native (Group 4) form of *Tridax* and the extract form of *Tridax* partially ameliorated (Group 6). Ashed form was not as effective as the native or extract forms of the *Tridax*.

Conclusion:
Tridax, especially native form exhibit amelioration of sucrose induce NAFLD, which contains calcium, magnesium, potassium, selenium, alkaloids, flavonoids, sponon, carotenoids and tannnians.Tridax has no residual toxicity. It can be safely included in the diet for early prevention of the diet induced NAFLD.

AMBULATORY BLOOD PRESSURE MONITORING IN PATIENTS WITH METABOLIC SYNDROME

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Aim:
Of this study was to investigate the clinical characteristics of arterial hypertension (AH) in patients with MS by ABPM.

Methods:
60 MS (36 men, mean age = 48±13 years, BMI = 33±5 kg/m^2, WCmen 114±11 cm, women 109±10 cm) and 20 AH lean subjects. All MS patients were insulin resistant, HOMA-IR = 5.8±3.6. AH diagnosed in 88.3 % (n=53) patients with MS. 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 AH in MS patients 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. AH 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 AH.

Conclusions:
Our study has 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.

ENDOTHELIAL FUNCTION AND PULSE-WAVE ANALYSIS IN PATIENTS WITH METABOLIC SYNDROME

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Purpose:
To evaluate changes in pulse-wave shape and endothelial function (EF) in patients with Metabolic syndrome treated with ACEi (ramipril) or calcium-channel blockers- (CCB).

Methods:
Sixty one patients (mean age 59±10 years) with MS were enrolled in the study and than randomized to ACEi or CCB-based regimen therapy. EF (in reactive hyperemia test) and pulse-wave characteristics were measured both before and after 5 weeks of treatment using novel finger photoplethysmographic device AngioScan-01 and traditional ultrasonographic method. Stiffness index (SI), reflection index (RI), augmentation index (AIx), systolic BP in aorta (SPa), digital pulse amplitude augmentation (by photoplethysmography), and flow-mediated dilation (FMD, by ultrasound) were accessed.

Results:
In the most of patients before the treatment normal SI, and elevated RI, AIx, Spa, and significantly impaired EF were shown. BP goals (< 130 and 90 mmHg) were achieved in all patients/. Decrease in SI ($p<.05$), RI and SPa were revealed in both treatment arms, whereas trends towards AIx decrease and EF improvement were demonstrated only in ramipril-treated patients.

Conclusions:
Pulse-wave analysis in patients with MS demonstrated pattern of increased vascular stiffness and peripheral

vasoconstriction, accompanying by impaired EF. Both ACEi and CCB treatment resulted in central BP and SI decrease, whereas only ACEi use was associated with trends in EF and AIx improvement in short-term follow-up.

RELATIONSHIP OF SERUM C - REACTIVE PROTEIN WITH INDICES OF METABOLIC SYNDROME AMONG NEWLY DIAGNOSED DIABETIC PAKISTANI SUBJECTS (TYPE 2 DIABETES)

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The C-reactive protein (CRP) is highly conserved and preferred marker of diabetes. This cross sectional study was conducted on newly diagnosed type 2 diabetic patients to evaluate the status of CRP with potential risk factors of diabetes including glycemic levels, obesity and lipid profile on their first visit to Amin Hayat Memorial Hospital Lahore. In this study a total of 150 subjects (males=90, females= 60) with age range 40-65 years were included. The subjects were stratified into 4 categories underweight, normal weight, overweight and obese subjects according to Asian standards. Different demographic parameters age, gender, BMI, waist circumference, WHR, B.P, personal history, socioeconomic status were recorded. Serum CRP level and Insulin level were assessed by ELISA technique. Fasting plasma glucose and HbA1c were measured by glucose oxidase and low pressure cation exchange chromatography and lipid profile were assessed by Hitachi chemical analyzer. It was concluded from the present study that serum CRP level (mg/L) and triglyceride level (mg/dl) were significantly higher in newly diagnosed type-2 diabetic subjects ($p < 0.05$). There was significant difference in the serum levels of CRP (mg/L) among underweight, normal weight, overweight and obese subjects ($p < 0.05$). CRP (mg/L) was significantly associated with glycemic levels and BMI($r = 0.98$, $p < 0.05$: $r = 0.123$, $p < 0.05$) respectively among diabetic subjects.

Keywords:
C-reactive protein, Diabetes, BMI and Metabolic syndrome.

THE PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH METABOLIC SYNDROME

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Introduction:
Non-alcoholic fatty liver disease (NAFLD) frequently occurs in Metabolic Syndrome (MS). However, the real prevalence of NAFLD in MS patients are not so well known. Aim of this study to evaluate the prevalence of NAFLD in MS patients

Methods:
60 IDF-criteria MS patients (36 men), age 48±13 years, BMI = 33±5 kg/m2, waist circumference men 114±11 cm, women 109±10 cm. Careful clinical examination, serum biochemistry (including ALT, AST, γ-GT, glucose, lipid spectrum, insulin measurements (mean HOMA-IR 5.8±3.6) and hepatitis screening), abdominal ultrasound diagnostics with precise liver assessment and liver biopsy.

Results:
In our study, NAFLD was found in 100% of included MS patients. Within group with confirmed NAFLD simple liver steatosis was diagnosed in 58 (n=35) %, non-alcoholic steatohepatitis (NASH) in 42 % (n=25) of MS patients. Liver biopsy was performed in 18 MS patients with elevated liver function tests and showed histological findings proven NASH. In the NASH group AST levels were 87.2 ± 46.5 IU/L, ALT 77.9 ± 34.4 IU/L, HOMA-IR = 6.6±4.1. These results demonstrated pathologic links between insulin resistant and NAFLD.

Conclusion:
We have shown that NAFLD is essential component and one of the diagnostic criteria of MS due to 100% prevalence in MS patients. NASH has very high prevalence (42 %) in MS patients. The attention should be given by physicians for focus NAFLD diagnosis in MS patients.

STRUCTURE OF THE LIVER DISEASE IN RUSSIAN FEDERATION NATIONAL-WIDE DIREG-L-01903 STUDY

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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.

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 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 %.

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

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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.

SEX-ASSOCIATED DIFFERENCES IN EFFECTS OF A DIETARY INTERVENTION ON ABDOMINAL OBESITY IN PATIENTS WITH METABOLIC SYNDROME

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Aim:
Assess short- and long-term effects of hypocaloric diet on abd obesity (AO) and gender compliance to diet in MS.

Methods:
60 IDF-criteria MS patients (36 men), age 48±13 years,BMI 33.4 ± 4.9 kg/m^2 both sexes; WC115.3 ± 11.3 cm men, 108.8 ± 9.6 cm women; WHR 1.02 ± 0.06 men, 1.00 ± 0.07 women. Compared AO anthropometric changes in Supervised 3 weeks short-term 1800 kkal programm and Home-based 6 months diet

Results:
At 3 weeks reducted in all AO measures in both sexes ($p < 0.0003$); men larger reducted in WC and WHR; Δ WC men 4.6 ± 1.7 cm vs Δ WC women 3.7 ± 2.1 cm; ΔWHR men 0.03 ± 0.01 vs ΔWHR women 0.027 ± 0.01. At 6 mth: less WC and WHR reductions-WC men 112.1±10.7 cm vs 110.6±10.4 cm; WC women 103.0 ± 6.9 cm vs 104.7±9.3 cm; WHR men 1.0 ± 0.05 vs 0.99±0.05; WHR women 0.96 ± 0.05 vs 0.98 ± 0.06. Compliance of Home diet related to sex (women better) and associated with greater reduction in WC and WHR in women. At 6 mth men increased in AO (Δ WC- 1.44±2.9 cm men, $p=0.02$; Δ WHR - 0.014 ± 0.02, $p=0.003$).

Conclusion:
Supervised short-term program is more effective than long Home-based diet. Predictive value of gender in outcomes: men greater reductions in WC and WHR in short-term supervised program, due to the less men compliance to the long-term home-based diet, women greater reducted in WC and WHR after 6 mths.

T2DM AND IGR RISKS AMONG ELDERLY PATIENTS WITH ESSENTIAL HYPERTENSION A 10-YEARS COHORT STUDY

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Objective:
To investigate the prevalence of T2DM and IGR among elderly patients with hypertension and without hypertension during 10 years' follow up.

Methods:
Objects of the cohort study are elderly patients(>60years) who had taken health examinations every year in our hospital, excluded previously diagnosed DM and IGR patients. Investigate the prevalence and risk factors by Kaplan-meier method and COX's Proportional Hazard Analysis.

Results:
Total investigated subjects was 1317, among which 582 subjects were enrolled in the study. There are 384 subjects in essential hypertension(HT) group and 198 subjects in non-essential hypertension(N-HT) group(including newly onset 67 hypertension subjects). During 10 years follow up, the newly onset diabetes was 27.6% in HT group and 18.7% in N-HT group(RR=1.66; 95%CI:1.09 2.52, P<0.05); incidence rate of DM among two group was 33.8‰ and 20.6‰ respectively. There is no difference in the prevalence of IGR among HT and N-HT group,and there has no difference in the prevalence of DM or IGR among newly onset HT group and N-HT group as well. The independent risk factors of T2DM was dyslipidemia(RR=1.459; 95%CI:1.027 2.072, P<0.05) and hypertension(RR=1.516; 95%CI:1.039 2.212, P<0.05) base on COX's Proportional Hazard Analysis. Dyslipidemia(RR=1.545; 95%CI:1.087 2.195, P<0.05) and hypertension(RR=1.524; 95%CI:1.044 2.224, P<0.05) are also independent risk factors of abnormal glycometabolism (T2DM and IGR). Kaplan-meier analysis indicates accumulative incidence of DM and abnormal glycometabolism are different between HT group and N-HT group.

Conclusion:
The DM risk is 1.66 folds higher in elderly patients with HT than in those without hypertention. Results from multivariate analysis indicates hypertension and dyslipidemia are independent risk factors of DM and abnormal glycometabolism (T2DM and IGR).

Key words:
elderly; essential hypertension; T2DM; IGR; risk factors; follow up

CORRELATION OF CAROTID INTIMA MEDIA THICKNESS (CIMT) WITH ATHEROSCLEROSIS RISK MARKERS IN TYPE 2 DIABETIC INDIAN PUNJABI POPULATION

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Aim:
We aimed to compare the correlation of various atherosclerotic risk markers in diabetes population with CIMT. Asian population is more susceptible to atherosclerotic heart disease as compared to other ethnic group.

Method:
In present study, 50 Type 2 diabetic patients (25M/25F) with an age between (30 – 70yrs.) having assessed the CIMT were recruited. CIMT and LVDD in all subjects was determined. Measurement of CIMT was measured on B- mode ultrasonography using high frequency linear transducer on a " LogiQ Book XP". BMI, WHR, HbA1c, Duration of diabetes, baPWV, Blood Pressure, Cholesterol, LDL, HDL, TGs of all the subjects were also measured. baPWV was measured with VP-2000/1000-Colin Corporation, (hyayashi komaki Japan).

Results:
The results showed that positive correlation of CIMT with Cholesterol (r = 0.32), SBP(r = 0.22), baPWV (r = 0.17), WHR (r = 0.18), BMI (r = 0.12), HbA1C (r = 0.16), but they could not achieve the level of statistical significance. LVDD, LDL, HDL, TGs, Duration of diabetes has not shown any correlation with CIMT.

Conclusion:
The study has proven that visceral fat and obesity with cholesterol showing are correlates with CIMT in uncontrolled Type 2 diabetic population. However, further larger studies needed to confirm other parameters also.

TO ASSESS THE LVDD BY 2DECHO & DOPPLER IN PATIENTS WITH TYPE2 DM IN SPECIFIC POPULATION

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Aim:
To Assess The Lvdd By 2Decho & Doppler In Patients With Type2 Dm In Specific Population.

Methods:
200 Type 2 pts., aged between 35-75 years were evaluated for LVDD using Doppler Echo. LVDD was determined by using conventional 2Decho and Doppler techniques & LVDD was graded as grade I, II, III & IV as per standard norms. Parameters such as Lipid Profile, HbA1c, Duration of diabetes, WHR, PWV, BP were also measured. LVEF was considered as a measure of systolic dysfunction.

Results:
LVDD was observed in 75% of patients. Predominant pattern was abnormal relaxation (58%) with highest incidence in age group 35 -73 yrs. Out of 200 patients studied, total 178 (89%) had LVDD, 128 patients (64%) had (Grade 1 DD), 30 patients (15.38%) had (Grade 2-), 20 patients (10%) had (Grade 3). 22 out (37.93%) had no diastolic dysfunction. LVDD had good correlation with duration of Diabetes (r = 0.30). LVDD also had good correlation with WHR (r = 0.20), HbA1C (r =0.20) and No significant correlation with PWV, Lipid profile and Blood pressure.

Conclusion:
The prevalence of LVDD is much common in this group of population. Since this is an early predictor of diabetes Heart disease, the presence of LVDD can act as a good screening marker for future Cardiac events.

THE COMBINATION OF URSODEOXYCHOLIC ACID AND SIMVASTATIN IN PATIENTS WITH DYSLIPIDEMIA AND METABOLIC SYNDROME

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Background and Aims:
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 from statin therapy would most likely outweigh any theoretical risk of liver injury. Combination of Ursodeoxycholic acid (UDCA,Ursosan) and simvastatin is perspective for the treatment dyslipidemia and NAFLD. Our aim was to assess the efficacy of Ursosan and simvastatin in MS patients with NAFLD and dyslipidemia.

Methods:
We examined 60 MS patients (36 men; average age 48±13 years; BMI=33.4 ± 4.9 kg/m^2; waist circumference=113.2 ± 11.1 cm) with clinic, laboratory, ultrasound proven

NAFLD and laboratory proven dyslipidemia. All paients were insulin resistant (mean HOMA-IR = 5.8±3.6).Liver biopsy was performed in 18 patients with elevated liver function tests and showed histological findings proven non-alcoholic steatohepatitis (NASH). All patients received Ursosan 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 Ursosan and simvastatin therapy. 94.5 % patients (n=17) with NASH reached normal liver function tests. All 60 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 ($p < 0.000006$).

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

PREVALENCE OF INSULIN RESISTANCE SYNDROME IN ADULTS FROM 8 DISTRICTS IN SOUTHINDIA ACCORDING TO ATP III DEFINITION

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Background and Aim:
In 2001, the Third Report of the National Cholesterol Education Program Adult Treatment Panel (ATP III) proposed a new definition for insulin resistance syndrome (IRS). The aim of this study was to estimate the prevalence of IRS in several districts in south india using ATP III criteria.

Material and Methods:
All studies of IRS prevalence in subjects 18 years of age or older, defined by ATP III, were included. Search was done up to August 201 0 in Internet database. Studies in special populations (offspring from diabetics, workers with high physical activity, athletes), and further studies with the same population were excluded (the study with the greater population was chosen). Studies in populations with extreme age ranges were also excluded. Finally, studies from 8 districts were analysed: Anantapur, Kadapa, Chittor, Vijayawada, Ongole, Khamam, Kurnool, and Nellore.

Results:
Data of 5492 subjects were collected. The prevalence of IRS was variable (12.7% - 38.7%). Overall prevalence was 21.3% (CI 95%: 14.9 - 27.7; n=66398). The distribution by sex was very similar (20.3% [CI: 13.8 - 26.9] and 22.4% [CI: 15.2 - 29.6] in men and in women, respectively; $p>0.05$.

Conclusions:
The prevalence of insulin resistance syndrome in the 8 districts studied was high and variable by ATP III definition. It is important to determine the global prevalence of this syndrome because it is a major problem of public health.

IMPACT OF SELF-REPORTED WEIGHT CHANGE ON QUALITY OF LIFE AMONG INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

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The SHIELD Study Group

Objective:
Weight loss, a key component of diabetes self-management, may lead to improved well-being. This study examined the association between self-reported weight change and quality of life (QOL) among individuals with type 2 diabetes mellitus (T2DM).

Methods:
In the US Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD) 2008 survey, respondents indicated whether they had lost or gained weight (any amount) compared with 1 year earlier and completed the SF-12 questionnaire and the SHIELD WQ-9 questionnaire indicating how weight change affected (improved or not improved) 9 aspects of their daily life (physical health, interactions with family, work performance, interactions with co-workers/friends, social activities, daily activities, self-esteem, emotional health, overall QOL). Respondents who reported gaining weight were compared with respondents who reported losing weight; those not reporting weight change were excluded.

Results:
Over 1 year, 16% of respondents reported gaining weight (n=460), and 30% reported losing weight (n=895). For all 9 aspects of daily life, a significantly greater proportion of respondents who reported losing weight reported improved well-being versus respondents who reported gaining weight (12%-44% vs <5%, respectively, p<0.0001 for each). For respondents reporting losing weight, the greatest proportions indicating improvement were for physical health, self-esteem, and overall QOL. SF-12 mental health scores but not physical health scores were significantly higher among respondents who reported losing weight than among those who reported gaining weight (p<0.001).

Conclusions:
Self-reported weight loss, compared with self-reported weight gain, was associated with improved QOL among individuals with T2DM.

IMPLICATIONS OF A TRADITIONAL CHINESE DIET ON ADIPONECTIN LEVELS IN AN ELDERLY CHINESE COHORT

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Objective:
To determine whether a traditional Chinese diet is associated with alterations in adiponectin levels, we examined a large cohort of elderly Chinese cross-sectionally.
Methods:
The subjects included 1,520 Chinese males and females over 50 years of age. Subject diet and adiponectin data was analysed non-parametrically (J-T and K-W tests) and parametrically (General Linear Model) for direct and secondary influence of dietary effects upon adiponectin levels.

Results:
In non-parametric analyses, only red meat was significant across all tests (standardised JT statistic=-3.639, p<0.001, K-W p=0.009). The General Linear Model showed no dietary influence on adiponectin levels. Three demographic variables found to be statistically significant; gender, BMI and age. Males had adiponectin levels 0.157pLg/ml less than females (95% CI=0.110-0.203, p<0.001). Each additional year of age resulted in an increase in adiponectin level of 0.004pLg/ml (95% CI=0.001-0.007, p=0.005). The only modifiable factor was BMI. Every increase of one BMI unit coincided with a reduction in adiponectin level by 0.026pLg/ml (95% CI=0.020-0.032). Oatmeal (p=0.022) and marinated vegetables (p=0.004) may influence adiponectin levels, via secondary mechanisms affecting BMI levels.

Conclusion:
Individual variables of a traditional Chinese diet do not profoundly influence adiponectin levels in elderly Chinese. We suggest further studies investigating a traditional Chinese diet in its combined form, and public health messages to lower national BMI levels, to reduce current increasing cardiovascular mortality, morbidity and financial strain in China.

Key words:
adiponectin, diet, Chinese, China, cardiovascular

METABOLIC STUDY OF SUBCLINICAL THYROID DISORDERS IN TYPE-2 DIABETES MELLITUS AMONG SOUTH INDIANS

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Objective:
The goal is, to determine the subclinical thyroid disorders that co-exist among type 2 Diabetes Mellitus(type-2DM) and co relate the metabolic study finding with subclinical hypothyroidism(SCH).

Background:
Clinical hypothyroidism and hyperthyroidism have been associated with type-2 DM. However data on the metabolic study in subclinical thyroid disorders among south Indian type-2DM is limited.

Methods:
We studied 110 type-2DM adults between 40-80 years. Age and gender matched individuals are compared to identify presence of thyroid disorders such as hypothyroidism, SCH, hyperthyroidism and metabolic dysfunction. Serum levels of T_3, T_4, TSH, FreeT_3, FreeT_4, TPO, fasting insulin along with glucose, lipid profile, HbA1c, urea, creatine, uric acid and liver enzymes were studied.

Results:
Groups from 110 type-2 DM were identified as Euthyroid group, 93%males and 74% females. SCH group, had of 4% and 20% and hypothyroid group had 4% and 6% males, females repectively. Increased TSH, Free T4 with p-value of 0.001 and positive TPO with a p-value of 0.007 was used for grouping. Metabolic dysfunction in SCH with higher BMI, Fasting insulin, glucose, total, LDL cholesterol, Triglycerides, Hba1c and Lower HDL cholesterol suggested onset of metabolic syndrome compared to euthyroid group, while hypothyroid group had significantly increased

Sub Clinical, Hypothyroid& Euthyroid Sample Of Type2-Dm				
Parameter	**Hypothyroid**	**Sub clinical hypothyroid**	**Euthyroid**	**P-Value**
HbA1c	8.84±3.40	7.85±1.87	8.00±2.15	0.674
Total- chol	224.20±96.69	175.53±27.78	165.01±37.58	0.007*
HDL-chol	37.30±11.10	36.66±8.89	39.09±7.24	0.516
LDL-chol	130.40±50.36	103.15±26.65	93.82±34.50	0.057
Triglyceride	296.00±278.25	171.15±67.64	167.29±91.12	0.027*
Urea	19.60±1.51	30.92±23.0	27.46±13.42	0.340
Creatinine	0.84±0.20	1.01±0.52	0.95±0.25	0.510
T3	1.11±0.49	1.53±0.24	1.62±0.37	0.010*
T4	53.84±20.65	95.06±17.55	92.08±19.06	<0.001*
TSH	17.03±16.12	5.61±1.43	2.02±0.99	<0.001*
FT3	2.56±0.63	2.83±0.68	3.01±0.87	0.426
FT4	0.86±0.23	1.19±0.19	1.25±0.18	<0.001*

TPO, Total & LDL Cholesterol, triglycerides and Hba1c suggesting progression of metabolic dysfunction.

Conclusions:
In 110 type-2 DM, 82.5% are euthyroid, 4.5% hypothyroid and 11.8%SCH. Free T_4 levels and positive serum TPO significantly demarcates between SCH and Hypothyroid. SCH group show evidence and onset of metabolic dysfunction and it is established in hypothyroid group.

EFFECT OF A CRANBERRY BEVERAGE ON INSULINOTROPIC RESPONSE IN MODERATELY HYPERCHOLESTEROLEMIC OVERWEIGHT/OBESE ADULTS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

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The rise in the obesity rates threaten to increase the risk of diabetes and cardiovascular disease. Early nutrition interventions that are geared to improving blood insulin and glucose in high risk populations are imperative. The objective of this study was to investigate the effect of a Cranberry Beverage on insulin and glucose levels in healthy adults with low to moderate risk according to the ATP-III criteria. This was a single-center, randomized, double-blind, placebo-controlled, parallel group study. A total of 280 subjects were consented and screened. A total of 140 eligible subjects aged 30-65 years (inclusive) were randomized equally with70 subjects in each of the two study arms: Cranberry Beverage or Placebo. The study product was supplied in the form of a beverage with phenolic content similar to commercially available cranberry juice. The calorie content per one 15.2 oz serving size was ≤ 20 kcal for both the test beverage and placebo. Subjects were to consume 2 bottles daily for a total of 30.4 oz per day for 12 weeks. The mean age of subjects in the intent-to-treat population in the Cranberry Beverage group was 48.3 ± 8.9 (Males 48.0 ± 7.2 years, Females 48.4 ± 9.2 years) and for placebo group was 47.7 ± 9.0 (Males 46.5 ± 9.5 years, Females 48.7 ± 8.7 years). SAS version 9.1 was used to perform the statistical analysis and probability values less than 0.05 were considered statistically significant. The area under the curve of glucose and insulin, total insulin secretion, and insulin sensitivity was calculated. There were no significant differences after 12 weeks of supplementation with Cranberry Beverage or placebo between groups for serum glucose response after a 2-hour oral glucose challenge. A significant reduction in insulin C_{max} and insulin AUC (P=0.004; P=0.001 respectively) from baseline to week 12 was seen in subjects on the Cranberry Beverage. There were no significant differences in liver function markers including AST, ALT and GGT, kidney function markers (eGFR), haematology or clinical chemistry parameters, vital signs between groups after 12 weeks of supplementation with either Cranberry Beverage or Placebo suggesting that the. Cranberry Beverage was well tolerated at the daily dose consumed for 12 weeks in the population studied. The results suggest that. dietary cranberry polyphenols may ameliorate insulin-sensitivity in moderately hypercholesterolemic overweight/obese-subjects. The molecular mechanisms remain still to be elucidated.

PlASMA OMENTIN-1 IN OBESE PRE-DIABETICS AND ITS RELATIONSHIP WITH INSULIN RESISTANCE

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Introduction:
Insulin resistance (IR) is increased in pre-diabetics (PD). Omentin-1 is a newly identified adipokine which is being implicated in glucose homeostasis. Plasma omentin-1 levels and its correlation with IR has not been studied in PD subjects of Indian origin.

Aims and objectives:
To determine IR and plasma omentin-1 in obese PD and obese normoglycemic subjects and to establish correlation of IR with omentin-1 in above mentioned groups and healthy controls.

Materials and methods:
Males (20-50yr) were divided in to 3 groups (G) of 30 each. Group I (Obese PD): Waist circumference (WC)>90 cm, having impaired glucose tolerance and/or impaired fasting glucose. Group II (Obese normoglycemic): WC>90 cm having normal glucose tolerance and normal fasting plasma glucose. Group III (healthy controls). Biochemical investigations-Fasting and postprandial plasma glucose (FPG, PPG), HbA1c, serum insulin, plasma omentin-1. IR was calculated by HOMA-IR.

Results:
Group I had significantly higher FPG, PPG, HbA1c compared to Group II and Group III ($p<0.001$). Fasting serum insulin was higher in Group I compared to Group II and Group III ($p<0.001$). HOMA-IR was higher in Group I compared to Group II ($p<0.001$). Plasma omentin-1 was lower in Group I compared to Group II ($p<0.005$). Omentin-1 showed significantly negative correlation with HOMA-IR ($p<0.009$).

Conclusion:
Omentin-1 has close association with obesity and IR. It's plasma concentration is deceased in obese PD. It has negative and significant correlation with IR. As Omentin increases sensitivity to insulin, its decreased levels in obese PD may be responsible for impaired glucose homeostasis.

IMPACT OF IL6 -G174C PROMOTER GENE POLYMORPHISM ON CIRCULATING IL6 LEVEL AND METABOLIC RISK MARKERS IN POLYCYSTIC OVARIAN SYNDROME

Objectives:
Polycystic ovary syndrome (PCOS) is considered to be multifaceted metabolic disorder. The present study was aimed to assess the IL6 -G174C gene polymorphism and its association with circulating IL6 level, Insulin Resistance (IR) and metabolic risk markers in north Indian PCOS women.

Design:
Case-control study.

Patients and Measurements:
A total of 298 women in the age group of 25±10 were enrolled for the present study, of which 126 were PCOS and 172 were non-PCOS women. Further, both the groups were categorized into obese and lean subgroups. Homeostatic Model Assessment (HOMA) index, circulatory IL6, DHEA, SHBG, Total Testosterone levels and lipid profile were analyzed in both the groups and subgroups. IL6-G174C genotyping was done by PCR-RFLP method.

Results:
We observed significantly high ($P<0.05$) frequency distribution of CC genotype ($p=<0.001$; OR=2.34; 95%CI=1.39-3.94), and C allele ($p=<0.004$; OR=1.83; 95%CI=1.32-2.55) in PCOS when compared with Non-PCOS group. Furthermore, on comparing obese and lean subgroups we observed significantly high ($P<0.05$) frequency distribution of CC genotype ($p=<0.029$; OR=2.84; 95%CI=1.18-6.80) and C allele ($p=<0.003$; OR=2.20; 95%CI=1.32-3.67) of IL6 -G174C gene polymorphism in obese subgroups. Furthermore, frequency distribution of mutant C allele of IL6 -G174C promoter gene polymorphism was found significantly higher in subjects having higher WHR ($p=<0.001$), HOMA index ($p=<0.001$), TC/HDL ($p=<0.002$) and serum IL6 level ($p=0.002$).

Conclusion:
These findings indicate that C allele at 174 position of IL-6 promoter gene and high circulatory level of IL6 are associated with obesity causing Insulin resistance which ultimately may cause metabolic syndrome irrespective of PCOS.

HOMA-INDEX, HIGH BLOOD PRESSURE AND METABOLIC SYNDROME IN PREDICTING CORONARY HEART DISEASE

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Introduction:
The impact of type 2 diabetes (DM) on coronary artery disease (CAD) is without doubt, but the ability to predict coronary heart disease using values of HOMA-index, arterial hypertension and metabolic syndrome is still unclear.

Methodology:
MetSy is defined by the IDF (International Diabetes Foundation) criteria. HOMA-index is calculated from the mathematical formulation from fasting glucose (FG) and insulin. Four groups were formed in relation to MetSy or HBP in the principle present/absent (group A(-MetSy/-HBP), B (+HBP/-MetSy), C(-HBP/+MetSy) and D (+HBP/+MetSy). CAD was graded according to angiography data, to had /did not have coronary stenosis or had one, two, three, four or more vessels disease.

Results:
Hundred eighty eight patients were evaluated after invasive cardiac. Average values of HOMA-index (9.05±8.36mmol/L) was significantly higher in the group with than in those without MetSy (HOMA (10.3 vs. 6mmol/L) ($p = 0.002$). HOMA was significantly higher in group D (10,6mmol/L) vs. C (7.8mmol/L) ($p = 0.0001$). Analyzing the relationship between HOMA-index and groups with HBP and MetSy, we concluded that HOMA-index, ware significantly higher in the group which had MetSy and hypertension than other groups ($p = 0.01$). Values of HOMA-index were higher in a group with three, four or more vessels disease, compared to those without CAD or who had one or two-vessel disease, but the difference was not statistically significant ($p = 0.587$).

Conclusion:
Patients with MetSy, with or without HBP, had statistically higher values of insulin resistance and more severe CAD, estimated by HOMA index, compared to the patients without MetSy.

ADEMETIONINE AND SIMVASTATIN IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE AND METABOLIC SYNDROME

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Background and Aims:
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 warry about prescribing statins. However, the benefits NAFLD and MS patients from statin therapy would most likely outweigh any theoretical risk of liver injury. Ademetionine (Heptral) belongs to a group of hepatoprotectors and exerts bile-expelling action, possesses detoxification, regeneration, antioxidative, antifibrotic properties in the liver. Combination of Ademetionine (Heptral) and simvastatin is perspective for the treatment dyslipidemia and NAFLD.

Our aim was to assess the efficacy of Heptral and simvastatin in MS patients with NAFLD and dyslipidemia.

Methods:
We examined 60 MS patients (36 men; average age 48±13 years; BMI=33.4 ± 4.9 kg/m^2; waist circumference=113.2 ± 11.1 cm) with clinic, laboratory, ultrasound proven NAFLD and laboratory proven dyslipidemia. All patients were insulinresistant (mean HOMA-IR = 5.8±3.6). Liver biopsy was performed in 25 patients with elevated liver function tests and showed histological findings proven nonalcoholic steatohepatitis (NASH). All patients received Heptral in doses of 800 mg/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 Heptral and simvastatin therapy. 92 % patients (n=23) with NASH reached normal liver function tests. All 60 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 ($p <0.000006$).

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

EFFECTS OF INSULIN RESISTANCE IN DIABETIC PATIENTS WITH CARDIOVASCULAR DISEASES

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Abstract:
The aim of this study was to evaluate the influence of different mean values of insulin resistance on cardiovascular diseases of patients with type 2 diabetes mellitus.

Methods:
We included 54 patients with type 2 diabetes (25 women and 28 men; age mean ± SD: 54 ± 9 years, duration of diabetes 7.2 ± 2.3 years, BMI = 32.9 ± 3.3 kg/m^2; 46 of them had HbA1c 8,3 ± 0.8% and 8 patients < 7%). The patients was evaluated for 1.5 years.

The evaluation of HOMAIR – score by HOMA2 calculator indicate several values that we concentrate them in 3 groups: ≈ 1.4; ≈ 1.7; ≈ 2.3.

The results indicate that the patients with HOMAIR ≈ 1.4 and HbA1c < 7% had only silent ischemic cardiomiopathy. At the same value of HOMAIR but with HbA1c = 8,3 ± 0.8%, 2 patients had angina pectoris. When HOMAIR grow at ≈ 1.7, the number of whose with angina pectoris increase to 5 patients when HbA1c < 7% and to 6 patients when HbA1c = 8.3 ± 0.8%.

When HOMAIR was ≈ 2.3, 8 patients with HbA1c < 7% had angina pectoris and 10 patients with HbA1c = 8.3 ± 0.8% had angina pectoris. In the period of evaluation none of the patients develop any other forms of ischemic cardiac disease.

The study demonstrated that the rise of angina pectoris increase primary with HOMAIR and secondary with the value of HbA1c. The rate cumulate when both HOMAIR and HbA1c are increased.

EFFECTS OF INSULIN RESISTANCE ON CEREBROVASCULAR DISEASES IN DIABETIC PATIENTS

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Abstract:
The aim of this study was to evaluate to the diabetic patients the influence of insulin resistance and HbA1c (both in different mean values) on ischemic cerebrovascular diseases.

Methods:
We included 23 patients with type 2 diabetes (12 men and 11 women; age mean ± SD: 58 ± 3 years; duration of diabetes 8.4 ± 3.2 years, BMI = 35.8 ± 2.9 kg/m^2). The number relative reduce of patients was done by the possibility of keep of HbA1c < 7%, who was able only to 23 patients from 84 at the begining of the trial. The patients with HbA1c < 7% was fallow up for 2 years, with no significant change in BMI.

We find using HOMA2 calculation different values of HOMAIR – score. We arbitrary selected those patients with HOMAIR – score about 2.8 (8 patients) and 3.2 (7 patients). In the first group, we observed the appearance at 2 patients (25%) of transition ischemic stroke and to another patients a definitive hemiparesis (12.5%).

In the group HOMAIR – score ≈ 3.2, we observed 3 (42.8 %) strokes with unreversibility of somatic mobility.

The study demonstrated that increase HOMA score represent an important factor of risk for the cerebrovascular disease even to the well balance diabetic.

MITOCHONDRIAL DYSFUNCTION IN SUBCUTANEOUS ADIPOSE TISSUE AND PERIPHERAL MONOCYTES IN PATIENTS WITH OBESITY AND TYPE 2 DIABETES MELLITUS: THE INFLUENCE OF VERY-LOW-CALORIE DIET

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Mitochondrial dysfunction has recently been associated with the development of insulin resistance and type

2 diabetes mellitus. The objective of this study was to evaluate the expression profile of selected genes reflecting mitochondrial activity in adipose tissue and peripheral monocytes of obese type 2 diabetic patients and to test the hypothesis that amelioration of mitochondrial dysfunction contributes to positive metabolic effects of short-term very low calorie diet (VLCD)

Thirteen obese females with type 2 diabetes mellitus (T2DM) and 12 healthy lean sex- and age-matched controls (C) were included into the study. The mRNA expression analysis of 8 genes encoding enzymes involved in tricarboxylic acid circle and oxidative phosphorylation was performed in samples of subcutaneous adipose tissue (SCAT) and peripheral monocytes (PM) using RT-PCR at baseline and after 2 weeks of VLCD (energy intake 2500 kJ/day). We assesed mRNA expression of genes for citrate synthase (CS), dihydrolipoamide S-acetyltransferase (DLAT), NADH dehydrogenase (ubiquinone) 1 alpha subcomplex 1 (NDUFA1), mitochondrially encoded NADH dehydrogenase 5 (MT-ND5), succinate dehydrogenase complex subunit A (SDHA), cytochrome c-1 (CYC1), cytochrome c oxidase subunit IV isoform 1 (COX4/1) and ATP synthase (ATPS).

Compared to C group, T2DM patients had significantly decreased mRNA expression of almost all mitochondrial genes except of NDUFA1 in SCAT. In PM a ~50 % reduction in expression of CS, MT-ND5 a NDUFA1 and a ~20% increase in expression of COX4/1 was observed. Two weeks of VLCD significantly decreased body weight and improved glycemia and insulin resistance. It also further decreased mRNA expression of MT-ND5 and SDHA in SCAT while no change in mitochondrial gene expression was observed in PM.

We conclude that T2DM is accompanied by mitochondrial dysfunction in both SCAT and PM. Short-term caloric restriction did not ameliorate this dysfunction in SCAT or PK despite significant weight loss and improvement of diabetes compensation and other metabolic parameters. Taken together, our data suggest that improvement of metabolic parameters after short-term caloric restriction in our patients cohort was not due to improvement of mitochondrial dysfunction in adipose tissue and circulating monocytes.

RESISTIN 420C/G GENE POLYMORPHISM WITH METABOLIC RISKS FACTORS IN POLYCYSTIC OVARIAN SYNDROME WOMEN

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The prevalence of polycystic ovary syndrome (PCOS) is very common in women of reproductive age. It is an endocrinological disorder, which may be associated with delineated metabolic implications. In the present study, we attempt to investigate the association of resistin 420C/G gene polymorphism with metabolic risks factors in polycystic ovarian women. A total number of 186 PCOS women (20-38years) and 170 age matched non-PCOS women were enrolled under this study. We estimated Homeostatic Model Assessment (HOMA) index, circulatory resistin, and lipid profiles. The genotyping of resistin- C420G were carried out using PCR-RFLP method. We found significant (p=<0.008 OR=1.79; 95% CI=1.72-2.73) frequency distribution of GG genotype. Moreover, G allele were also found to be significant (p=<0.012; OR=1.51; 95%CI=1.10-2.08) in PCOS as compared to age matched non-PCOS women. The frequency distribution of mutant G allele of resistin 420- C/G promoter gene polymorphism proportionate to the level of WHR (p=<0.001), HOMA index (p=<0.001), TC/HDL (p=<0.003) and circulating resistin (p=0.004) in PCOS women.

On the basis of these observations, it may conclude that G allele at 420 position of resistin promoter gene and high circulatory level of resistin are associated with the metabolic risk factors like insulin resistance (HOMA index), obesity and dyslipedemia. Thus PCOS women with GG mutant genotype and G allele are more prone for development of metabolic syndrome.

ANTIOXIDANT ACTIVITY AND PROTECTION OF PANCREATIC β-CELLS BY EMBELIN IN EXPERIMENTAL DIABETES

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Aim of the present study was to evaluate the antidiabetic as well as antioxidant potential of embelin in

streptozotocin-induced diabetes. Streptozotocin diabetes caused highly significant variations in blood, serum and tissue biochemical parameters of rats. Following embelin administration at the dose levels of 15, 25 and 30 mg kg/b. wt./day to diabetic rats a highly significant decline in the blood glycated hemoglobin and serum glucose levels and nitric oxide activity with concomitant increase in serum insulin concentration was observed. Furthermore, embelin treatment increased the pancreatic antioxidant enzyme status (superoxide dismutase, catalase, reduced glutathione, glutathione peroxidase, glutathione *S*-transferase and ascorbic acid) and also decreased the thiobarbituric acid-reactive oxygen species contents. The histoarchitecture of diabetic rats showed the degenerated pancreas with less β-cells counts, while embelin treatment significantly regenerated islets cells. In conclusion, present study suggests that diabetes is associated with decreased antioxidant ambiance through oxidative stress and embelin treatment is effective in managing the diabetes.

Keywords:
Antioxidant; Diabetes; Embelica ribes; Serum insulin; Thiobarbituric acid-reactive oxygen species.

RELATIONSHIP OF IL-10 WITH OBESITY AND INSULIN SENSITIVITY IN OBESE DIABETIC PAKISTANI WOMEN

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Obesity is accompanied by a state of low-grade systemic inflammation that may contribute to insulin resistance. Obesity is a condition of inflammation in which adipose tissue produce several chemokines and cytokines. Obesity is epidemic problem globally and results in insulin resistance, type 2 diabetes, hypertension and cardiovascular disease. The study was based on the normal weight, overweight and obese diabetic women. The present study was conducted to assess the IL-10 level in the serum of diabetic women of different BMI groups. The women with age ranging between 35-70 years were included in the study with mean BMI 27.9 ± 0.49 kg/m^2.Other parameters like fasting blood glucose, systolic and diastolic blood pressure, HbA1c and lipid profile were also included in the study. The IL-10 concentration and fasting serum insulin was measured by ELISA and its relation was found with study parameters. Insulin sensitivity and insulin resistance (HOMA-IR) were calculated. It was found that IL-10 concentration in the serum was negatively correlated with BMI kg/m^2 ($r = -0.526$, $p < 0.01$) and WHR ($r = -0.266$, $p < 0.05$).A positive correlation was observed between IL-10 and insulin sensitivity ($r = 0.494$, $p < 0.01$). Insulin sensitivity significantly decreased with increase in weight ($r = -0.237$, $p < 0.05$), waist ($r = -0.355$, $p < 0.01$) and WHR ($r = 0.266$, $p < 0.05$).

Key words:
IL-10, obesity, insulin resistance, Type 2 diabetes.

Acknowledgement:
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ASSOCIATION OF HOMA-IR AND HOMA-BETA WITH SERUM TRIGLYCERIDE LEVELS IN HCV SERONEGATIVE HEROIN ADDICTS

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Background:
The research studies announce development of Insulin resistance (IR) in opioid use due to the serine ^{612} fosforilation of IRS-1 (1). IR induces dyslipidemia presented with increased Gl and decreased HDL –C concentrations. The aim of the study is to evaluate the differences in HOMA-IR and HOMA-beta indexes considering TGl levels in HCV seronegative heroin dependents with referent BMI.

Results:
The study included 83 heroin addicts divided in 2 groups according their TGL levels: group 1 (N=50) with TGL < 1, 7 mmol/l and group 2 with Tgl ≥ 1, 7 mmol/l (N=33) compared to the control group (N=31) of healthy volunteers. The IDF cut -off criteria for metabolic syndrome considering TGL and waist circumference were used. IR was calculated using HOMA-IR and HOMA-beta model (2). The group with higher TGL levels showed higher levels of HOMA- IR (3,38± 3,61) and HOMA – beta (196,15± 186,10) compared to the group with lower TGL (HOMA-IR=1,87± 2,00 and HOMA-beta =122,30 ±163,95) and control group (HOMAIR= 1,24 ± 0,53 and HOMA-beta 67,51 ±28,87). The differences were statistically significant for HOMA-IR (df=2, F= 5,137, p=0,007) and HOMA-beta= (df=2, F= 7,026 p=0,001) between the control group and group 2 as well as between the two groups of addicts. Linear regression analysis showed significant association of waist circumference with HOMA-IR (p=0,005).

Conclusion:
Heroin dependents with increased TGL show increased IR, beta cell production, making a preconditioning for developing a metabolic syndrome. Increased waist circumference contributes to higher levels of IR in heroin addicts despite referent BMI.

RELATIONSHIP OF TNF- α WITH INSULIN RESISTANCE AND OTHER PARAMETERS OF METABOLIC SYNDROME AMONG TYPE 2 DIABETIC PAKISTANI SUBJECTS

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Diabetes mellitus is a multifactorial disorder. Cytokines secreted by the monocyte-macrophage system play a key role in the pathogenesis of type 2 diabetes. Pro-inflammatory cytokine TNF-α is believed to have an important role in the progression of diabetes. The present study was conducted to assess the level of TNF-α and to find its relationship with insulin sensitivity and other indicators of metabolic syndrome among newly diagnosed type II diabetic subjects. 100 diabetic subjects (age; 48.63±0.92, BMI; 28.51±0.52) were included in the study. Four groups were made on the basis of BMI as normal weight, overweight, moderately obese, severely obese subjects. Different demographic parameters as age, BMI, B.P, personal history and socioeconomic status were recorded. Fasting glucose, random glucose, HbA1c and lipid profile were analyzed by chemistry analyzer. Serum insulin and plasma TNF-α levels were assessed by ELISA. Insulin sensitivity and insulin resistance was calculated. ANOVA revealed significant difference between TNF-α among different BMI groups ($P<0.05$). On correlation analysis, TNF-α was significantly correlated with BMI, WHR and TG ($p<0.01$). Severely obese subjects had higher insulin level and a strong correlation was observed between plasma TNF-α and serum insulin ($p<0.01$). TNF-α was significantly correlated with insulin sensitivity ($p<0.05$). TNF-α was significantly associated with insulin resistance ($p<0.01$). TNF-α was also negatively correlated with HDL ($p<0.05$) while non-significant relationship was observed between TNF-α and HbA1c, systolic B.P, diastolic B.P, Cholesterol and LDL ($p>0.05$).

Key words:
TNF-α, insulin resistance, obesity, type 2 diabetes, metabolic syndrome

INTERLEUKIN-6 IS SIGNIFICANTLY ASSOCIATED WITH INSULIN RESISTANCE AMONG TYPE 2 DIABETIC PAKISTANI SUBJECTS

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Rapid increase in the incidence of diabetes mellitus is one of the most serious and challenging health problems. Obesity is a risk factor for type 2 diabetes and insulin resistance. The present study was conducted to assess the serum concentration of IL-6 and determine its relationship with insulin resistance among newly diagnosed type 2 diabetic subjects. Patients with age group 37-75 years, (both sexes) were included in the study. Out of which 54 were males and 46 were females. On the basis of BMI three groups were made as normal weight (n= 23), over weight (n=46) and obese (n= 31). Different demographic parameters as age, BMI, WHR, blood pressure, personal history and socioeconomic status were recorded. The biochemical parameters including fasting blood glucose, random blood glucose, HbA1c, lipid profile were assessed by chemistry analyzer while serum IL-6, IL-8 and insulin level was assessed by ELISA. Insulin resistance was measured by HOMA-IR. The concentration of IL-6 (pg/mL) was elevated among the three BMI groups but significantly high levels of IL-6 were observed in obese group ($p < 0.05$). IL-6 showed significant association with insulin resistance ($p < 0.05$). This underscores the significance of inflammatory marker IL-6 in newly diagnosed diabetic subjects and describes its association with insulin resistance.

Key words:
IL-6, IL-8, Type 2 diabetes, insulin resistance.

CIRCULATING CYTOKINES, CHEMOKINES AND ADHESION MOLECULES IN EUGLYCEMIC GESTATIONAL DIABETES

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Gestational diabetes mellitus (GDM), a pathological state of carbohydrate intolerance first recognized during

pregnancy, when left untreated leads to an increased risk of severe complications with an excessive maternal inflammatory response. In order to investigate the role of GDM in the inflammatory activation, we determined levels of circulating inflammatory markers under euglycemic conditions in 12 women with GDM (32,08+1,59 yo) and 9 matched for age nondiabetic mothers (NGD) (29,5+1,84 yo), by a multiple bead array with internally colour-codes microspheres amid fluorescent dyes excited by laser beams. All pregnancies were uncomplicated with normal newborns. The GDM group demonstrated significantly higher serum insulin levels than NGD (12,06+1,7 vs 7,28+0,94 μIU/ml) (p<0,02), while at the same euglycemic levels indicating an insulin resistance state for GDM mothers. HbA1c levels of GDM were within normal limits (4,5+0,4%). There was no difference in the BMI of GDM vs NGD before pregnancy (25,92+1,2 vs 24,25+1,9) as well as for the weight gained during pregnancy between the groups (10,96+1,5 vs 13,8+3,6 kg). Circulating concentrations of ICAM-1 (210,85+10,9 vs 141,66+9,8 ng/ml) (p<0,0015), E-Selectin (31,67+4,4 vs 12,55+2,6 ng/ml) (p<0,0073) and IFN-γ (182,95+61,2 vs 27,61+7,9 pg/ml) (p<0,036) were markedly increased in the GDM group than NGD, while VCAM-1, TNF-α and IL-12(p70) levels were comparable. Circulating levels of IL-1β, IL-2, IL-6, IL-8, IL-10, and IL-12(p40) were undetectable in both groups. In conclusion, in GDM, an insulin resistance state even in euglycemic conditions, there is a mainly endothelial pro-inflammatory environment illustrated by the notably elevated endothelial inflammatory markers.

ASSOCIATION OF INFLAMMATORY MARKERS WITH INDICATORS OF CARDIOVASCULAR DISEASE AMONG TYPE 2 DIABETIC PAKISTANI SUBJECTS

Sadaf Farasat, Tasnim Farasat

The proinflammatory cytokines IL-6, IL-8 and TNF-α have been suggested to affect insulin signaling. The present study was conducted to assess the serum concentration of IL-6, IL-8, and TNF-α and determine its relationship with insulin resistance and other parameters of cardiovascular disease among diabetic subjects. This cross sectional study was conducted on 350 newly diagnosed type 2 diabetic patients who attended diabetic Clinics in Lahore from December 2010 - August 2011. Patients with age group 38-65 years, (both sexes) were included in the study. Respecting the Asian criteria of obesity the subjects were grouped as normal weight, overweight and obese. Different demographic parameters age, BMI, WHR, B.P, personal history and socioeconomic status were recorded. The biochemical parameters including fasting blood glucose, random blood glucose HbA1c, lipid profile were assessed by chemistry analyzer while serum concentrations of IL-6, IL-8 TNF-α and insulin level were assessed by ELISA. Insulin resistance was measured by HOMA-IR. The levels of IL-6, IL-8, TNF-α and insulin were elevated among the overweight and obese groups but significant increase in the level of IL-6 was observed in obese group ($p < 0.05$). IL-8 was significantly correlated with BMI and fasting blood glucose ($r=3.62$, $p < 0.05$). TNF-α was significantly correlated with insulin resistance (r=0.541p 0.01) irrespective of BMI. A significant association of IL-6 and TNF-α with WHR, lipid profile, fasting insulin and insulin resistance was observed ($p < 0.05$). Inflammation may play a crucial role in the obesity associated health complications such as dyslipidemia, insulin resistance and hypertension leading to cardiovascular diseases.

Key words:
Key words: IL-6, IL-8, TNF Type 2 diabetes, insulin resistance CVD.

GLUCOREGULATION IN DIABETIC PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Objectives:
Obstructive sleep apnea (OSA) is associated with obesity, hyperglycemia, and diabetes mellitus (DM). The hyperglycemia may be due to increased sympathetic activity from overnight apnea. Uncontrolled DM, as well as hypoglycemia (HYPO), can lead to further autonomic dysfunction. Therefore, we evaluated whether glucose regulation is affected by autonomic function in male DM with symptomatic OSA.

Methods:
We conducted a retrospective chart review of 77 male DM [(21 Type 1: 56 Type 2) (29 OSA+: 48 OSA-) (Age= 63±1.3yrs) (BMI=33.3±0.85) (Duration DM= 18.0 ±11.3yrs) (HbA1c=7.95±1.7%) (Bezett QTc=439±5.0mm)] with glucose assessments via the 72hr continuous glucose monitoring system (CGMS). Values were mathematically transformed into % time above normal (>140 mg%) (%AN), % normal (70-140 mg%) (%N), and % below normal (<70 mg%) (%BN) for 3 time intervals: (T1=0600-1800hrs); (T2=1800-2400hrs); (T3=2400-0600hrs). Glucose averages for 72 hr time period were also calculated.

Results:
OSA+ patients with QTc<440 had overall more HYPO than those with QTc>440 mm (6±2 vs 2±1%; p<0.05), as well as for all time periods (T1=6±2 vs 2± 1% ;p<.06),(T2

=7±3 vs 2±1%;p< 0.05), and (T3=7± 2 vs 1±1%;p< 0.05). Patients without OSA had no significant differences for HYPO, based upon QTc. DM with OSA had a higher BMI than those without OSA (p<0.01).

Conclusions:
Despite similar HbA1c and BMI, patients with OSA and QTc<440mm had more overall hypoglycemia than patients with QTc >440mm, suggesting that glucoregulation may depend upon the integrity of the autonomic nervous system. Therefore it is important to evaluate autonomic function when recommending a regimen of tight glycemic control.

Supported by JAL FHCC

METABOLIC SYNDROME AND HOMOCYSTEINE LEVELS IN LATIN POPULATION

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To determine the difference in homocysteine levels (HcyL) in subjects with and without metabolic syndrome (MS), and the relationship between HcyL and components of MS, total cholesterol, LDL -C and body mass index (BMI).

Methods:
A total of 71 workers (consecutive) of a hospital in Lima-Perú (23 men and 48 women) with no past history of diabetes mellitus, cardiovascular disease, hipertension or stroke were studied. MS was diagnosed according to the International Diabetes Federation criteria. Variables: Components of the MS (waist circumference, triglycerides, HDL-C, blood pressure, fasting blood glucose), HcyL, total cholesterol, LDL- C and BMI. Plasma HcyL was determined with Competitive Immunoassay.

Results:
The mean age was 39,83 ± 7,37 (males) and 46,25 ± 9,35 (females). Twenty two subjects had MS (30,98%). Mean HcyL was 11, 1 ± 6,54 umol/l in the MS group and 8,5 ± 2,55 umol/l in the non-MS group (p = 0,136). HcyL increase was directly related to the number of MS components (1 to 3) but unrelated to MS diagnosis.

We observed increase in HcyL in relation to increase in triglycerides (p = 0,009), waist circumference (p = 0,015), total cholesterol (p = 0,06) and LDL -C (p = 0,05). We did not find relationship between HcyL and HDL-C, blood pressure, fasting glucose or BMI.

Conclusions:
There was no significant difference in the mean levels of HcyL in subjects with or without MS. HcyL levels may relate to the number of MS components. Increased waist circumference, total cholesterol, triglycerides and LDL cholesterol relates to an increase in HcyL.

VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) EXPRESSION IS REDUCED IN ADIPOSE TISSUE OF INSULIN-RESISTANT VERSUS INSULIN-SENSITIVE HUMANS

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Objective:
It has been shown that adipose tissue in obese versus lean humans is hypoxic, with lower capillary density, and decreased activation of hypoxia-responsive, angiogenic genes. We sought to test the hypothesis that abnormal response to hypoxia in adipose tissue is related to insulin resistance by comparing angiogenic gene expression in insulin-resistant versus equally obese insulin-sensitive humans.

Methods:
To test this hypothesis, 18 overweight/obese, nondiabetic individuals (9 insulin-resistant and 9 insulin-sensitive) underwent insulin sensitivity testing and biopsy of abdominal subcutaneous adipose tissue. Insulin sensitivity was quantified in these subjects by the modified insulin suppression test by determining their steady state plasma glucose concentrations. Gene expression for hypoxia responsive genes in adipose tissue were measured and compared. Results: Adipose tissue of overweight/obese, insulin-resistant humans had lower expression of VEGF (0.63 ± 0.23 vs. 0.97 ± 0.19, p=0.003) and PPAR-gamma (0.70 ± 0.18 vs. 1.04 ± 0.21 p=0.002) when compared to equally-overweight/obese insulin-sensitive humans. There was a strong positive correlation between VEGF and PPAR-gamma expression (r = 0.79, p<0.001).

Conclusion:
Overall, insulin resistance is characterized by a maladaptive response to hypoxia, which may be related to decreased PPAR-gamma and/or VEGF expression in subcutaneous adipose tissue. Given prior research showing that PPAR-gamma agonists can stimulate VEGF expression in vitro and in mice, and that angiogenesis and adipogenesis are coupled during adipose tissue expansion, it is plausible that

a defect in one or both may underlie the development of insulin resistance associated with human obesity. Further research in this area is warranted.

MEASUREMENT OF INSULIN-MEDIATED GLUCOSE UPTAKE: DIRECT COMPARISON OF THE MODIFIED INSULIN SUPPRESSION TEST AND THE EUGLYCEMIC, HYPERINSULINEMIC CLAMP

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Introduction:
Peripheral sensitivity to insulin varies several-fold in apparently healthy individuals and is largely determined at the genetic level. Two direct measures of whole body insulin sensitivity are the *M* value derived from the euglycemic, hyperinsulinemic clamp and the steady state plasma glucose (SSPG) derived from the insulin suppression test (IST). Our study goals were to quantify the relationship between SSPG and *M* in the same individuals and to determine by how much these measures of insulin-mediated glucose uptake (IMGU) agreed with each other.

Methods:
We studied 18 subjects whose mean ±SD age was 52±7 years; BMI, 28.6±4.2 kg/m^2; and fasting glucose, 5.90±0.67 mmol/L. The subjects underwent a euglycemic, hyperinsulinemic clamp test and a modified IST within a median interval of 7 days. We employed correlation and linear regression analyses to quantify the relationship between SSPG and *M* and Bland-Altman plots to examine the agreement between the two measures of insulin sensitivity.

Results:
The SSPG concentrations varied ~5-fold (3.50–17.26 mmol/L) and the *M* values varied ~9-fold (9.56–90.21 μmol/min/kg-LBM). There was a highly significant correlation between SSPG concentration and *M* (Spearman's rho = -0.91, P <0.001). Furthermore, Bland-Altman plots demonstrated a good agreement between these two methodologies.

Conclusion:
The measurements of IMGU by the IST and euglycemic, hyperinsulinemic clamp are highly correlated and exhibit a good agreement with each other. We propose that large-scale studies of the genetic basis of insulin sensitivity can gain power by combining IMGU measurements by the IST with those by the euglycemic, hyperinsulinemic clamp.

ACANTHOSIS NIGRICANS ASSOCIATED WITH METABOLIC SYNDROME AS A CARDIOVASCULAR RISK FACTOR PRESENT IN POLYCYSTIC OVARY SYNDROME

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Context: Hormonal and metabolic factors in polycystic ovary syndrome (PCOS) influence each other. The classical endocrine dysfunction in PCOS may be aggravated by insulin resistance and its signals as the so called components of metabolic syndrome (MS). Moreover, attention has turned to acanthosis nigricans (AN) as a cutaneous manifestation indicative of increased risk for the development of insulin resistance and diabetes. Objective: To further understand the cardiovascular risk based in the relationship between MS and AN as constituents of phenotypic heterogeneity concerning PCOS. Methods: Prospective descriptive analysis. A total of 104 consecutive PCOS women were diagnosed based on the latest 2003 Rotterdam consensus and the MS according to the classification stipulated by Grundy et al. (2005). AN was identified by the presence of dark, thick, velvety, pigmented skin, in most cases (over 70%) in the neck. Results: The average age at diagnosis, the mean body mass index (BMI) and waist circumference from this cohort were 25.30 years, 29.78 and 91.20 cm respectively. Over 62% were classified as overweight or obese. Specifically, looking at prevalence of MS and AN, 37.5% and 50% respectively, should be considered that the incidence of AN related to MS (82.1%) (32 cases) was significant (p<0.001). The same was not true in relation to their hirsutism (p= 0.227) and acne (p= 0.768). Conclusion: It is worth mentioning the extraordinary prevalence of AN associated with MS and, by extension, in particular, one may perhaps consider the high cardiovascular risk present in PCOS.

PREVALENCE OF INSULIN RESISTANCE AMONG ASTHMATICS

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Background:
The prevalence of asthma appears to be increased in overweight/obese individuals. It also appears that patients with asthma or asthma-like symptoms have an increased prevalence of prediabetes and metabolic syndrome. Some research has concluded that insulin resistance is a stronger predictor of asthma-like symptoms than obesity. However, the link between obesity, insulin resistance and asthma is not clear and the role of insulin resistance in the pathogenesis of asthma has not been well defined.

Methods:
We sought to determine the prevalence of insulin resistance (IR) in asthmatics. We conducted a retrospective review of volunteer individuals from our IR studies from 1999-2009. Inclusion criteria were asthma documented in the past medical history or use of an inhaler. Exclusion criteria were other airway disease or history of prolonged tobacco use. We used the steady-state plasma glucose (SSPG) concentration from the insulin suppression test to categorize insulin resistance (SSPG >180 mg/dL) and insulin sensitivity (<180 mg/dL).

Results:
From this database we identified 57 individuals, 91% who were overweight/obese. Of these 57 individuals, 56% were classified as IR, including 16% with fasting plasma glucose >126 mg/dL. This prevalence of IR is essentially twice that as compared to a group of obese non-asthmatic individuals as demonstrated in our prior research.

Conclusions:
The prevalence of insulin resistance is increased in overweight/obese asthmatics as compared with apparently healthy individuals as studied in the past by our research group. These findings raise the possibility that improving insulin sensitivity might provide clinical benefit in patients with asthma.

CORRELATION OF LIPOPROTEIN PARAMETERS IN A LARGE CARDIOLOGY PREVENTION COMMUNITY DATABASE

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Objective:
The triglyceride to HDL ratio (TG/HDL) and LDL pattern B have been reported to be associated with an atherogenic profile and insulin resistance. We sought to study the correlation of these lipid parameters in subjects with 'normal' levels of TG and HDL in a large prevention cardiology community database.

Methods:
De-identified patient records between January 2010 and May 2011 from a mixed ethnic and gender prevention cardiology outpatient database (Berkeley HeartLab, Alameda, CA) were selected for HDL measures of >40 and < 60 mg/dL and triglycerides >70 and < 160 mg/dL. LDL pattern (A, AB and B) was determined by gradient gel electrophoresis. TG/HDL ratio > 3.5 was investigated as a correlate for LDL pattern B.

Results:
24,407 patient records met study criteria. The lipid measures for LDL patterns A, AB and B were, respectively (mean mg/dL (std dev)): non-HDL (131 (38), 130 (38), 118 (33); ApoB (84 (21), 86 (22), 81 (19)); HDL-C (50 (6), 47 (5), 47 (5)); triglycerides (106 (24), 123 (24), 129 (22)), TG/HDL (2.2 (0.6), 2.6 (0.6), 2.8 (0.6)). Mean TG, HDL-C, and TG/HDL differed ($p<0.05$) among the three patterns but not ApoB and non-HDL. Patients with TG/HDL > 3.5, a correlate for insulin resistance, constituted 2, 8 and 14% of pattern A, AB, and B, respectively. Pattern B is consistently higher in males.

Conclusions:
LDL patterns do not differ significantly for all lipoprotein measures in the selected population. The TG/HDL ratio is not well correlated with pattern B for this subset of patients.

QUESTIONING THE ROLE OF VITAMIN D IN INSULIN RESISTANCE

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Background:
Over the past several years considerable evidence has raised the possibility that optimizing Vitamin D levels may play a role in decreasing the risk of progression to type 2 diabetes (T2DM). However, cross-sectional and longitudinal studies fail to achieve a consensus about the association between vitamin D status and T2DM-related parameters. We sought to assess the impact of difference in plasma Vitamin D concentration on insulin resistance.

Methods:
We conducted the insulin suppression test in a group of 78 apparently healthy individuals in order to calculate the steady-state plasma glucose (SSPG) concentration and quantify insulin mediated glucose disposal. Based on prior validated data, we divided individuals into insulin resistant (IR) and insulin sensitive (IS) subgroups, and obese (OB) and normal weight (NW) subgroups. We then created three experimental groups: normal weight-IS, obese-IS, and obese-IR matched for all but one relevant experimental variable. Finally, we compared 25-OH Vitamin D (25-OHD) concentrations among the groups.

Results:
We found that plasma 25-OHD concentrations were essentially identical in all three experimental groups, (p=0.25) irrespective of substantial differences in either adiposity or insulin sensitivity. Furthermore, at least 33% of each subgroup had 25-OHD insufficiency or deficiency (≤30 ng/mL). We also found that there was no significant difference in SSPG concentration between those with low versus normal 25-OHD levels within each subgroup (obese-IS p=0.36, obese-IR p=0.34).

Conclusions:
Differences in plasma 25-OHD concentration do not appear to play an important role in the modulation of insulin-mediated glucose disposal, and thus the development of type 2 diabetes.

INSULIN RESISTANCE IS ATTENUATED IN MEXICAN INDIVIDUALS PRESENTING PPARG2 PRO12ALA POLYMORPHISM

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Background:
Insulin resistance is the basis underlying multiple pathological states. PPARG2 is a transcription factor involved in adipocyte differentiation and the regulation of lipid metabolism. It has been suggested that Pro12Ala polymorphism of PPARG2 could influence tissue insulin sensitivity.

Objective:
To determine the association of Pro12Ala polymorphism with insulin resistance with in a group of obese individuals.

Patients and Methods:
77 Mexican individuals from the west of Mexico were studied. Polymorphism was determined by PCR-RFLP's. Anthropometric and biochemical variables were collected. Results were analyzed through Student-t-Test and Chi-square test.

Results:
We studied 52 women and 25 men. Pro12 and Ala12 alleles were present in 90% and 10% of the subjects. Most of the subjects (79.2%) presented the homozygous genotype Pro12Pro. Ala12Ala genotype was lacking in this population. Pro12Pro genotype showed direct association with body mass index, as it was statistically higher ($p<0.05$) in Pro12Pro genotyped women (30.5±4.1 kg/m^2) than in Pro12Ala genotyped women (27.5±4 kg/m^2). Body fat composition in Pro12Pro genotyped women (40.2±3.1%) was statistically higher ($p<0.05$) than in heterozygous women (37.6±3.7%). Most (92.3%) of the normoinsulinemic subjects (<15μU/ml) were heterocygous compared with wild genotype (63%) and the difference was statistically significant ($p<0.05$). HOMA was statistically higher ($p<0.05$) in those individuals Pro12Pro (3.3 ± 2.1) than in heterocigous subjects (1.7 ± 0.6).

Conclusions:
In this study, association of the polymorphic allele Ala12 with a better insulin sensitivity pattern and a healthier body

fat distribution was observed. Higher number of individuals should be analyzed in order to obtain more evident conclusions.

NITRIC OXIDE (NO)/CGMP-DEPENDENT PROTEIN KINASE TYPE-I (PKG-I) SIGNALING PATHWAY REGULATES FAT CELL DIFFERENTIATION: RELEVANCE TO OBESITY AND THE ONSET OF TYPE II DIABETES

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Dysfunction of the NO/cGMP/PKG-I signaling pathway is directly linked with the proclivity of cardiovascular complications associated with diabetes and obesity. Previously, our laboratory had shown PKG-I was the key kinase activated by the ubiquitous small-molecule NO in airway and vascular smooth muscle cells, leading to airway/vascular relaxation. Our more recent studies with ovarian and lung cancer cells have shown that PKG-I has pro-growth and anti-apoptotic/cytoprotective effects. Cellular responses to NO are highly-dependent on local NO concentrations, with "physiological levels" (picomolar levels) serving a protective role and high-nanomolar/micromolar levels having cytotoxic/pathological effects. Furthermore, the two isoforms of PKG-I (PKG-Iα and PKG-Iβ) are differentially activated based on NO levels (PKG-Iα requiring picomolar and PKG-Iβ requiring low-nanomolar levels). Here, we determined the expression and possible role of PKG-I in fat-cell differentiation (adipogenesis). Specifically, we determined PKG-I isoform-expression profile in lipid-poor and lipid-rich cells and investigated NO/cGMP/PKG-I involvement in adipogenesis. Although PKG-I is easily detectable in some cells, other cells express relatively low PKG-I levels, making it difficult to detect via conventional Western blot. Our studies use the novel NanoPro100 system, an automated capillary-electrophoresis-chemoluminescence-based-immuno-quantification instrument, which provides much higher sensitivity, phospho-protein-resolving power and quantification, compared with conventional Western blots. We found fat-cell differentiation caused a dramatic decrease in PKG-I expression though PKG-Iβ expression was preserved, corresponding with increased accumulation of NO in lipid-rich cells. Additionally, stimulators/inhibitors of the NO/cGMP/PKG-I pathway substantially changed lipid accumulation, suggesting a key role of this pathway in the development of obesity, potentially linking PKG-I to the pathogenesis of Type II diabetes.

COULD WE IDENTIFY PATIENT WHO HAD AN INCREASED RISK OF CAD – WHAT IS IMPORTANT, ANALYSIS OF INDIVIDUAL RISK FACTORS OR METABOLIC SYNDROME ALONE?

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Introduction:
One of the important questions which still remain open is its predictive value: does the MetSy predicted coronary artery disease and its progression any better than the sum of individual components?

Objective:
To assess the impact of metabolic syndrome in the prediction of coronary heart disease compared to standard coronary risk factors.

Methodology:
MetSy was defined according to the IDF International Diabetes Foundation criteria (IDF). It is important to analyze the impact of individual, standard risk factors for CAD, in relation to the metabolic syndrome, in terms of prediction of CAD.

Results:
The study included 594 consecutive patients who had CAD. Binary logistic regression examined the possibility of the existence of CAD prediction based on a set of predictor variables (gender, age, BMI, waist circumference, diabetes or glucose intolerance, high blood pressure, fasting glucose, low ejection fraction, symptoms of unstable or stable angina pectoris, syndrome angina pectoris (atypical chest pain with positive exercise test), metabolic syndrome, heredity, hyperlipidemia). The contribution of this set of predictor variables for predicting coronary heart disease was statistically significant ($p < 0.001$). The success of the logistic model in predicting the existence of CAD was 83%. Statistically significances in predicting CAD gave the existence of the following predictor variables: waist circumference ($p<0.01$), type 2 diabetes ($p<0,03$), smoking ($p<0.01$), which increases the chances of CAD incidence

and angina pectoris syndrome (p<0.001), which reduces the chances of CAD incidence.

Conclusion:
We concluded that chances for CAD was greater in obese patients with type 2 diabetes who used tabacco.

XMETA, A GLUCOREGULATORY MONOCLONAL ANTIBODY TO THE HUMAN INSULIN RECEPTOR

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Many type-2 diabetes mellitus (T2DM) patients with insulin resistance (IR) require basal insulin therapy to maintain normal fasting glucose levels. However, there is evidence that hyperinsulinemia in combination with IR leads to T2DM complications. In order to develop a novel treatment for these individuals, we employed phage display technology to target the insulin receptor (INSR), and identified a high affinity, fully human, monoclonal antibody, XMetA, which mimicked only the glucoregulatory action of insulin. Biophysical studies with cells expressing human INSR demonstrated that XMetA acted allosterically, and did not compete with insulin for binding to its receptor. In cultured cells, this antibody acted as a partial agonist of the INSR, eliciting tyrosine phosphorylation of INSR but not the IGF-1R. While this antibody activated metabolic signaling, leading to enhanced glucose uptake, it did not induce mitogenesis of either normal or cancer cells. XMetA was evaluated for activity in an insulin resistant, insulinopenic model of T2DM, the multi-low dose streptozotocin, high-fat diet mouse. Marked reduction of elevated fasting blood glucose levels and normalization of glucose tolerance were observed with doses of XMetA as low as 1.0 mg/kg. After six weeks of treatment there was a significant improvement in HbA1c levels. In contrast to insulin treatment, hypoglycemia and weight gain were not observed during these studies. XMetA also improved multiple markers of dyslipidemia. Therefore, human monoclonal antibodies have the potential to be novel, ultra-long acting, agents for the regulation of hyperglycemia in T2DM.

CONTROVERSY ABOUT THE METABOLIC SYNDROME ARE STILL PRESENT – SINGLE CENTER EXPERIENCE WITH PREDICTION OF CORONARY ARTERY DISEASE

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Introduction:
The impact of metabolic syndrome in predicting coronary artery disease (CAD) is controversial and directly correlated to the recommended criteria and choice of population groups.

Methodology:
MetSy definition met the International Diabetes Foundation (IDF) criteria. Four groups were formed in relation to MetSy or type 2 diabetes mellitus (DM) in the principle of present/absent (group A(-MetSy/-DM), B(DM+/-MetSy), C(-DM/+MetSy) and D(+DM/+MetSy). Patients were analyzed in relation to invasive cardiac diagnostic findings to those who had or did not have CAD.

Results:
The study included 837 consecutive patients, who performed invasive cardiac diagnosis (mean age 60±8.7 y., 77% were male). Of the total number of patients included in the study 75.6%(632) met the criteria for MetSy, type 2 diabetes had a 22.8%, elevated fasting glucose had 60% of patients. MetSy was more often present in those with three blood vessels disease (bvd.)(non 18%, one 25% vs. two 21% vs. three 31% vs. four bvd. 4%), but not significantly (p=0.088). Group C, was the most common (one 40% vs. two 38% vs. three 39% vs. four bvd. 26%), especially in patients whithout CAD (50%). Percentage of patients from D group, were statistically significant increases due to more severe degree of CAD (one 32% vs. two 36% vs. three 42% vs. four 47% bvd.) or in those who did not have CAD (22%)(Chi-square=28:84, df=12, p=0.004).

Conclusion:
Type 2 diabetes is a significant predictor of coronary heart disease and severe degree of CAD compared to the group with MetSy who did not include DM.

CORRELATION OF CIRCULATING ADIPOKINE WITH ANTHROPOMETRIC, LIPID PROFILE AND METABOLIC RISK FACTORS IN ADULT WOMEN WITH METABOLIC SYNDROME

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Background:
Metabolic Syndrome is one of the commonest risk factors for cardiovascular mortality.

Objective:
To explore the association of circulating adipokine with anthropometric, lipid profile and metabolic risk factors in north Indian metabolic syndrome women.

Methods:
Total 541 women were recruited into two groups; 272 women without metabolic syndrome (wMetS; control) and according to the NCEPATP III criteria 269 women with metabolic syndrome (MetS; study) were enrolled. ELISA technique was employed to determine the serum adipokine (IL-6, TNF-α, Resistin, Leptin and adiponectin) level. The fasting blood glucose, fasting insulin and lipid profile were detected by commercially available kits. Insulin resistance was calculated by the homeostasis model assessment (HOMA) index-2.

Results:
The circulating levels of adipokines was significantly higher (all $p<0.001$) except low adiponectin level (20.21±10.85 vs. 29.56±13.46 ng/ml; $p<0.001$) for MetS women compared to wMetS. All adipokine are positively correlated with waist circumference, waist to hip ratio, BMI, total cholesterol, triglyceride, HDL-C and Insulin while negatively with adiponectin level. Adiponectin was found to be inverse/negative correlation with risk factors (glucose, waist circumference, systolic and diastolic blood pressure, triglyceride), total cholesterol, LDL-C, TC/HDL-C, insulin and with adipokine level i.e. IL-6, TNF-α, Resistin, Leptin (all $p<0.01$) whereas positive correlation with HDL-C ($r=0.20$; $p<0.01$).

Conclusions:
These result concluded that adipokines originated from adipose tissue might take part in the progression of metabolic syndrome.

Keywords:
Adipokine, lipid profile, risk factors, metabolic syndrome

RELATIONSHIP BETWEEN INSULIN RESISTANCE AND CIRCULATING LEVELS OF RESISTIN AND ADIPONECTIN IN METABOLIC SYNDROME WOMEN OF NORTH INDIA

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Objective:
The aim is to study the relationship between insulin resistance and circulating adiponectin and resistin level in women with metabolic syndrome.

Methods:
A total 269 women with metabolic syndrome (MetS; study) according the criteria of National Cholesterol education Program-Adult treatment Panel III (NCEP-ATP), 2001 and 272 women without metabolic syndrome (wMetS; control) were enrolled and serum adiponectin and resistin were measured for this cross sectional case control study.

Results:
Compared with wMetS women, higher fasting plasma insulin (8.48±5.79 vs. 12.24±8.42 μU/ml) and higher insulin resistance (1.93±1.39 vs. 3.31±2.58) by homeostasis model (HOMA-IR) were found in MetS women (all $p<0.001$). The circulating levels of resistin in MetS women and wMetS was 13.96 and 9.56 ng/ml with a significant difference ($P<0.001$) while the low adiponectin level (20.21 and 29.56 ng/ml) in MetS women as compared to wMetS women. Significant correlations between insulin resistance parameter and BMI, waist circumference, waist-to-hip ratio, serum total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol, TC/HDL-cholesterol, resistin and adiponectin levels (all $p<0.01$) were noted. On performing multiple regression analysis for the relationship between Insulin resistance and one or more predictor variables, we found significant association for SBP, DBP, TC/HDL-Cholesterol, adiponectin level (all $p<0.05$) and fasting glucose and Insulin (all $p<0.001$), but not with resistin ($p>0.05$).

Conclusions:
These results suggest that adiponectin may play a protective role in metabolic syndrome through decreasing insulin resistance.

Key words:
Adiponectin, Insulin resistance, metabolic syndrome, Resistin.

CORRELATION OF CIRCULATING LEPTIN WITH LIPID PROFILE, INSULIN RESISTANCE AND ADIPOKINE LEVEL IN WOMEN WITH METABOLIC SYNDROME OF NORTH INDIA

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Background:
Leptin plays an important role in the regulation of body weight and it operates by inhibiting food intake, stimulating energy expenditure and deficiency in leptin leads to metabolic syndrome.

Objective:
The purpose of the study is to explore the correlation of serum leptin with adipokine level, lipid profile and Insulin resistance (IR) in metabolic syndrome women of north India.

Method:
Serum level of adipokine, lipid profile and IR were measured with the help of radio-immuno assay (RIA) or enzyme-linked immune-sorbent assay (ELISA). Pearson correlation coefficient (r) analysis was used to determine the correlation of circulating leptin level. Total subjects (n=541) divided into 269 women with metabolic syndrome (MetS; study) according the criteria of National Cholesterol education Program-Adult treatment Panel III (NCEP-ATP), 2001 and 272 women without metabolic syndrome (wMetS; control) were selected.

Result:
The serum level of leptin was found significantly higher in MetS women (15.77±10.47 vs. 9.56±6.88 ng/ml; $p<0.001$) as compared to wMetS women. Correlation (r) between increased serum leptin level and waist circumference (WC), waist-to-hip ratio (WHR), body mass index (BMI), Diastolic blood pressure (DBP), Glucose and Insulin, lipid profile i.e. TC (r=0.12), HDL-C (r=0.01), TG (r=0.08), LDL-C (r=0.11), TC/HDL-C ratio (r=0.09), HOMA-IR (r=0.19) and high adipokine level {IL-6 (r=0.25), TNF-α (r=0.44) and resistin (r=0.55)} was strong positive while highly significant negative correlation with low serum adiponectin level (r=-0.37, $p<0.001$) in MetS women.

Conclusion:
These finding suggests that MetS women have high circulating leptin level is likely to be more significantly correlated with altered level of adipokine, Insulin resistance and metabolic syndrome related risk factors.

Keywords:
Leptin; Insulin resistance; Lipid profile; Metabolic syndrome.

HOMA-INDEX, HIGH BLOOD PRESSURE AND METABOLIC SYNDROME IN PREDICTING CORONARY HEART DISEASE

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Introduction:
The impact of type 2 diabetes (DM) on coronary artery disease (CAD) is without doubt, but the ability to predict coronary heart disease using values of HOMA-index, arterial hypertension and metabolic syndrome is still unclear.

Methodology:
MetSy is defined by the IDF (International Diabetes Foundation) criteria. HOMA-index is calculated from the mathematical formulation from fasting glucose (FG) and insulin. Four groups were formed in relation to MetSy or HBP in the principle present/absent (group A (-MetSy/-HBP), B (+HBP/-MetSy), C (-HBP/+MetSy) and D (+HBP/+MetSy). CAD was graded according to angiography data, to had /did not have coronary stenosis or had one, two, three, four or more vessels disease.

Results:
Hundred eighty eight patients were evaluated after invasive cardiac. Average values of HOMA-index

(9.05±8.36mmol/L) was significantly higher in the group with than in those without MetSy (HOMA (10.3 vs. 6mmol/L)(p = 0.002). HOMA was significantly higher in group D (10,6mmol/L) vs. C (7.8mmol/L) (p = 0.0001). Analyzing the relationship between HOMA-index and groups with HBP and MetSy, we concluded that HOMA-index, ware significantly higher in the group which had MetSy and hypertension than other groups (p = 0.01). Values of HOMA-index were higher in a group with three, four or more vessels disease, compared to those without CAD or who had one or two-vessel disease, but the difference was not statistically significant (p = 0.587).

Conclusion:
Patients with MetSy, with or without HBP, had statistically higher values of insulin resistance and more severe CAD, estimated by HOMA index, compared to the patients without MetSy.

ASSOCIATIONS BETWEEN OBESITY, LIPID PROFILE, INSULIN RESISTANCE, GLUCOSE LEVEL AND TSH IN A LATIN AMERICAN POPULATION

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Objective:
To investigate the associations between insulin resistance, glucose level, lipid profile, body mass index (BMI), waist circumference and TSH level in a Peruvian urban population.

Methods:
Cross-sectional study. 101 volunteers (66 women and 35 men) with no history of thyroid disease, cardiovascular disease or diabetes were included. Oral glucose tolerance test (OGTT), fasting insulin, lipid profile (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides), TSH, BMI and waist circumference were assessed. The level of insulin resistance was estimated by the homeostasis model assessment for insulin resistance (HOMA-IR).

Results:
The mean age of the participants was 52.1±7.6 years with a BMI of 29.6±5.6 kg/m^2. TSH levels were positively correlated with HOMA-IR (r=0.287, p=0.004), 2-hour glucose levels during OGTT (r = 0.256, p=0.010) and BMI (r = 0.220, p=0.027). There was no correlation between lipid levels, fasting glucose, waist circumference and TSH levels. A generalized linear model adjusted for sex and age revealed that only HOMA-IR contributed significantly to the variance of TSH (p=0.045).

Conclusions:
A relationship between TSH and obesity may exist, mainly influenced by insulin resistance. We didn't find the classical association between an important cardiometabolic risk factor like lipid levels and TSH.

ADIPONECTIN GENE EXPRESSION IN ADIPOSE TISSUE OF OBESE SUBJECTS

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Background:
Adiponectin is a recently described adipokine that has been recognized as a key regulator of insulin sensitivity. Studies of isolated human explants or adipocytes suggest that there is no difference in adiponectin secretion from visceral or subcutaneous depots. Early evidence suggesting that adiponectin expression may be reduced in states of obesity. Therefore, controversies in the depot specific expression still exist. Depot-specific adiponectin mRNA levels could be relevant to obesity associated diseases and physiological functions.

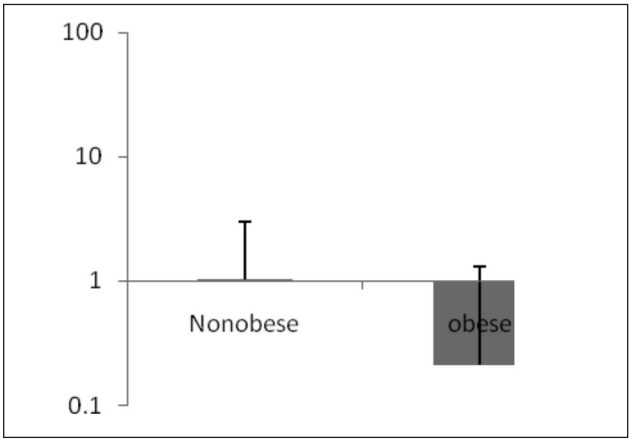

Fig. 1. VAT vs. VAT

Objective:
The purpose of this study was to compare adiponectin mRNA expression in visceral and subcutaneous adipose tissue in postmenopausal women with and without obesity.

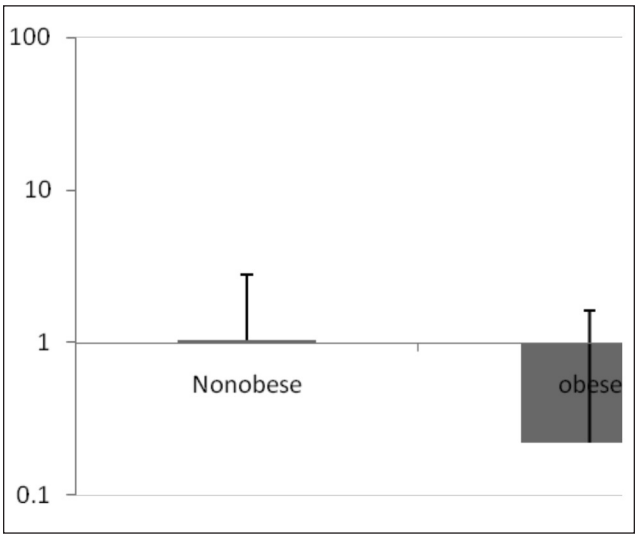

Fig. 2. SAT vs SAT

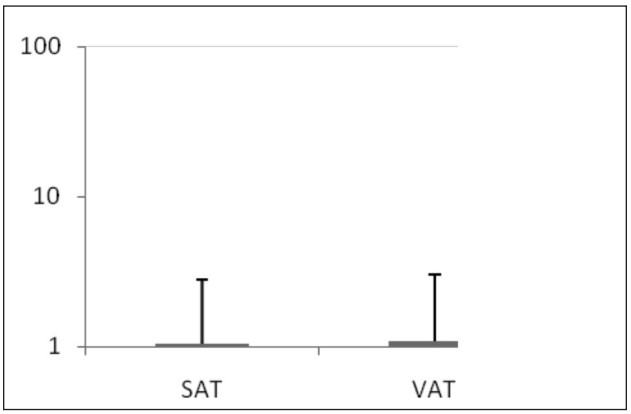

Fig. 3. SAT Vs. VAT (non obese)

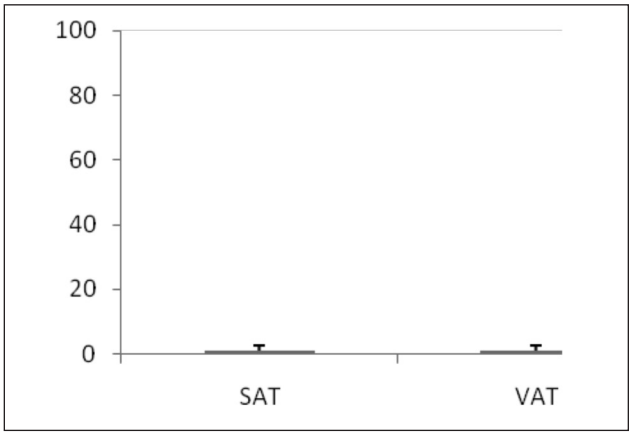

Fig. 4. SAT vs. Vat (Obese)

Methods:
This case control study was carried out on (n=10, postmenopausal women), in which five were obese (mean BMI 33.98 ± 4.05 kg/m2) and five were non obese (mean BMI 21.97 ± 3.27kg/m2) and the mean age was 55.06 ± 6.91 yr. Visceral and subcutaneous adipose tissues (VAT and SAT) were obtained from subject undergoing open abdominal surgery at CSM Medical University, Lucknow, India. Adiponectin mRNA expression was measured by Real Time-RT PCR.

Results:
There was significantly lower adiponectin mRNA expression in VAT in obese as compared to non obese. We also observed significantly lower expression of adiponectin mRNA in SAT of obese subjects as compared to non obese subject. There was no significant difference in adiponectin mRNA expression between VAT and SAT in both the groups.

Conclusion:
In summary, our findings suggest that visceral adipose tissue show a lower adiponectin expression in obese as compared to non obese.

DIABETES IS A MARKER FOR ADVERSE IN-HOSPITAL CARDIOVASCULAR OUTCOMES: ANALYSIS OF NATIONAL REGISTRY OF MYOCARDIAL INFARCTION 4-5

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Background
Diabetes is a recognized risk factor for cardiovascular (CV) disease and is associated with adverse outcomes in patients with acute coronary syndromes. However, the impact of diabetes, specifically on inpatient CV morbidity and mortality is not well understood in patients with acute myocardial infarction (AMI).

Methods
Analyses were conducted using data from 232,927 National Registry of Myocardial Infarction (NRMI 4-5) patients hospitalized for AMI between July 2002 and December 2006 with data collected through discharge. Multivariable logistic regression analyses were performed to evaluate the association between diabetes status and in-hospital adverse outcomes including all-cause mortality, recurrent myocardial infarction (MI), and stroke. Adjustment for covariates included demographic characteristics, previous medical

history, AMI characteristics, and pre-admission medications. The interaction between diabetes and history of prior MI was also tested.

Results
Within the cohort, 31% had a history of diabetes. Females accounted for 45% of patients with diabetes and 39% of patients without diabetes. ST-segment elevation myocardial infarction (STEMI) occurred in 31% of patients with diabetes and 40% of those without diabetes. Patients with diabetes reported higher use of pre-admission CV medications, including ACE inhibitors/ARBs, lipid-lowering agents, antiplatelet agent, and beta blockers. Patients with diabetes had an increased adjusted risk of in-hospital mortality, recurrent MI, and stroke, with no interaction between diabetes status and history of prior MI.

In-Hospital Cardiovascular Outcomes in Patients With and Without Diabetes

In-Hospital Outcome	Event Rate, % (n)		Adjusted Odds Ratio (OR)	95% Confidence Interval	p-value
	Diabetes (n=71,358)	No Diabetes (n=161,569)			
Mortality	10.1% (7,177)	8.3% (13,372)	1.23	1.18, 1.28	<0.001
Recurrent MI	1.5% (1,102)	1.3% (2,046)	1.14	1.05, 1.24	0.002
Stroke	1.4% (970)	1.0% (1,636)	1.29	1.17, 1.41	<0.001

Conclusion
Patients with diabetes presenting with an AMI are an increased risk of subsequent in-hospital adverse events, including mortality, recurrent MI and stroke. These findings highlight the need for appropriate management and new treatment options to prevent and reduce CV events in patients with AMI, particularly in those with diabetes.

METABOLIC SYNDROME AND HOMOCYSTEINE LEVELS IN LATIN POPULATION

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Objective:
To determine the difference in homocysteine levels (HcyL) in subjects with and without metabolic syndrome (MS), and the relationship between HcyL and components of MS, total cholesterol, LDL -C and body mass index (BMI).

Methods:
A total of 71 workers (consecutive) of a hospital in Lima-Perú (23 men and 48 women) with no past history of diabetes mellitus, cardiovascular disease, hipertension or stroke were studied. MS was diagnosed according to the International Diabetes Federation criteria. Variables: Components of the MS (waist circumference, triglycerides, HDL-C, blood pressure, fasting blood glucose), HcyL, total cholesterol, LDL- C and BMI. Plasma HcyL was determined with Competitive Immunoassay.

Results:
The mean age was 39,83 ± 7,37 (males) and 46,25 ± 9,35 (females). Twenty two subjects had MS (30,98%). Mean HcyL was 11, 1 ± 6,54 umol/l in the MS group and 8,5 ± 2,55 umol/l in the non-MS group (p = 0,136). HcyL increase was directly related to the number of MS components (1 to 3) but unrelated to MS diagnosis.

We observed increase in HcyL in relation to increase in triglycerides (p = 0,009), waist circumference (p = 0,015), total cholesterol (p = 0,06) and LDL -C (p = 0,05). We did not find relationship between HcyL and HDL-C, blood pressure, fasting glucose or BMI.

Conclusions:
There was no significant difference in the mean levels of HcyL in subjects with or without MS. HcyL levels may relate to the number of MS components. Increased waist circumference, total cholesterol, triglycerides and LDL cholesterol relates to an increase in HcyL.

HEART AND SKELETAL MUSCLE INSULIN RESISTANCE DURING TROGLITAZONE THERAPY IN TYPE-2 DIABETES

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Background
An existence of insulin resistance (IR) in the heart has been reported. Improvement of heart and skeletal muscle insulin resistance after thiazolidinediones therapy (rosiglitazone, pioglitazone) has been reported in patients with type II diabetes (T2DM). However, effects of troglitazone on heart and skeletal muscle IR has been remain uncertain.

Aim:
We hypothesized that effects of troglitazone could provide different results in T2DM without CAD, we aimed to clarify the heart and skeletal muscle and whole body IR in T2DM without CAD during within 12 week's troglitazone therapy (TRO).

Method:
We analyzed data of 15 T2DM to whom dynamic PET with ^{18}F-FDG under insulin clamping had been undertaken before and after TRO (200 mg/day). Data were compared with 17 age-matched controls.

Results:
Whole body glucose disposal rate (WBGR mg/min/kg) in T2DM (3.41±1.72) was significantly lower than that of controls (9.76±2.97 p<0.01) as was the skeletal muscle glucose utilization rate (SMGU mg/min/kg); T2DM 0.367±0.217 vs. Controls 1.34±0.613 p<0.01) and myocardial glucose utilization rate (MGU mg/min/kg; T2DM 5.86±2.03 vs. Controls 7.34±1.80, p<0.05). WBGR in T2DM after TRO (5.17±2.75 p<0.05) was significantly higher than that before initiation of TRO, as was the SMGU (0.782±0.20, p<0.05). MGU in T2DM after TRO (6.59±0.72) was comparable with that before initiation of TRO.

Conclusion:
Myocardial IR in response to TRO differ from skeletal muscle and the whole body IR response to TRO in T2DM without CAD.

RELATIONSHIP BETWEEN BODY MASS INDEX, WAIST CIRCUMFERENCE, LIPID PROFILE AND INSULIN RESISTANCE INDEX (HOMA-IR) LEVELS IN PERUVIAN ADOLESCENT GIRLS

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Objective:
To examine the relationship between body mass index (BMI), waist circumference, lipid profile and insulin resistance in a Peruvian adolescent female population.

Methods:
Cross-sectional study of 134 healthy adolescents aged 13 - 17 years. Fasting insulin, glucose, lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides), BMI and waist circumference were measured. Insulin resistance was evaluated by the homeostasis model assessment of insulin resistance (HOMA-IR). Overweight and obesity status were determined by using the age and sex specific BMI reference data of Must *et al*.

Results:
The mean age of the participants was 15.1±0.9 years. We found that the prevalence of overweight was 25.9% and obesity was 11.1%. HOMA-IR was positively correlated with BMI (r=0.207, p=0.017) and waist circumference (r=0.219, p=0.011). There was no correlation between HOMA-IR and lipid levels: total cholesterol (r=0.042, p=0.63), LDL cholesterol (r=0.061, p=0.44), HDL cholesterol (r=0.135, p=0.12) and triglycerides (r=0.141, p=0.10). In multiple regression analysis, only waist circumference was strongly associated with HOMA-IR (p=0.014).

Conclusion:
Waist circumference seems to be the best anthropometric parameter associated with insulin resistance in Peruvian adolescent girls. It is necessary to define the appropriate cut-off points of waist circumference for school-aged children in Peru.

PREVALENCE OF METABOLIC SYNDROME AND ITS COMPONENTS IN PERUVIAN POPULATION UNDER 1000 M AND OVER 3000 M

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Objective:
To determine and compare the prevalence of metabolic syndrome (MetS) and its components in Peruvian population under 1000 m and over 3000 m.

Methods:
Population-based cross-sectional study. We included 2150 participants aged 20 years old and above, 1230 under 1000 m (level-1) and 920 over 3000 m (level-2). MetS was defined according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria.

Results:
The prevalence of MetS was significantly higher in level-1 (19.7%) than in level-2 (10.2%), p<0.001. In males the prevalence was 9.2% in level-1 and 5.1% in level-2. In females was 29.9% in level-1 compared to 15.2% in level-2. Central obesity (35.5% vs 21.1%), elevated blood pressure (20.9% vs 15.0%), hyperglycemia (3.9% vs 1.7%), raised triglycerides (31.3% vs 25.7%) and low concentrations of HDLc (57.4% vs 52.5%) were significantly more prevalent in level-1 compared to level-2 (p<0.05). The most frequent components of MetS in men were hypertriglyceridemia and low HDLc, and in women were low HDLc and central obesity.

Conclusions:
MetS were significantly more prevalent in population under 1000 m; it may be as result of the nutritional, demographic, and socioeconomic transition in this area. Women were more susceptible to these cardiovascular risk factors.

METFORMIN THERAPY REDUCES THE DEVELOPMENT HOMA$_{IR}$ IN STREPTOZOTOCIN INDUCED TYPE I DIABETIC WISTAR RATS

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Background:
Insulin resistance (HOMA$_{IR}$) is considered as a complicated metabolic defect. Although Type 1 diabetes mellitus (T1DM) is an autoimmune disorder insulin resistance is also present at receptor level. Traditionally type 1 diabetes mellitus is managed by exogenous insulin therapy and this is also reported that hyperinsulinemia desensitizes the insulin action. The insulin resistance states may lead to diabetic co-morbidities like cardiovascular disorders.

Objective:
We studied the effects of metformin along with insulin therapy on the development of HOMA$_{IR}$ in T1DM Wistar rats. The percent change in BMI during an experiment period of 30 days and chemical variables including fasting blood glucose (FBS), Serum Hexosamine, Fasting Insulin levels and HOMA$_{IR}$ were evaluated. **Methodology:** Six weeks old male wistar rats were made type 1 diabetic models with streptozotocin; they were equally grouped in Group1 with single drug insulin therapy and Group 2 with combined metformin and insulin drug therapy. The chemical parameters were assessed on the day 0 when hyperglycemia was achieved. The chemical variables were determined three times with a 10 day interval during a month. The insulin resistance was calculated by the formula.

Results:
One way ANOVA showed a significant effect of combined therapy on HOMA$_{IR}$ between both the groups with respect to time ($F_{1,15}$ =152.511; P < 0.000 on day 10), ($F_{1,15}$ =54.110; P < 0.000 on day 20) and ($F_{1,15}$ =58.635;P< 0.000 on day 30). The percent changes in BMI (p<0.01), FBS (p<0.01) and hexosamine (p<0.01) were also significantly reduced in the animals treated with combined therapy.

Discussion:
The drug metformin reduces the fasting circulating levels of glucose, hexosamine and insulin. It also delays the development and severity of HOMA$_{IR}$. Further studies are recommended on the subject.

RANDOM EXAMINATION OF BLOOD GLUCOSE IN ADULTS BY TRAINED VOLUNTEERS IN A HOSPITAL SETTING

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Background:
Screening for dysglycemia, diabetes and hypertension can be conducted by trained volunteers in a public location and may identify incident cases of these conditions.

Objective:
To examine the incidence of dysglycemia and diabetes among screened, non hospitalized subjects in a hospital setting.

Methods:
A diabetes and hypertension screening station staffed by trained volunteers was placed in a central location at E. Wolfson Medical Center, Holon. Volunteers measured height, weight, blood glucose (by glucometer) and blood pressure (by sphygmomanometer). Screened subjects were asked whether they had diabetes. Normoglycemia was defined as glucose level <140mg%, dysglycemia as 140-190mg% and diabetes as ≥200mg%. Screening was performed free of charge.

Results:
A total of 1401 individuals (50.3% females, 53±15.1 years) underwent screening. Of these, 228 reported known diabetes and 136 reported known hypertension. In the 1173 subjects without known diabetes, dysglycemia was detected in 247 (21.1%) adults and diabetes was found in 51 (4.3%) subjects. Compared to normoglycemic subjects, individuals with dysglycemia were significantly older (58.0±14 vs. 52.7±15.1 years, p<0.001), had significantly higher blood glucose (179.7±46.9 vs. 109.3±16.1 mg/dl, p<0.001), BMI 28.5±6.1 vs. 27.3±5 kg/m^2, p<0.001), and systolic blood pressure (132±27mmHg vs. 126±25mmHg, p<0.004). Patients with newly identified diabetes had significantly higher blood glucose (251.3±57.2 vs. 118.6±25.5 mg/dl, p<0.001), but did not significantly differ in terms of age, BMI or blood pressure.

Conclusion:
Implementation of a screening processes in public places can identify diabetes and dysglycemia conditions which require further medical evaluation.

TREATMENT OF HYPERTRIGLYCERIDEMIC PANCREATITIS WITH SUBCUTANEOUS INSULIN AND HEPARIN

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Hypertriglyceridemia is a rare cause of pancreatitis. Hyperlipidemic pancreatitis occurs more often in patients with poorly controlled or untreated diabetes (in both Type I and Type II diabetics).

18 year old female with past medical history of diabetes mellitus on glipizide and hypothyroidism on synthroid 50 mcg came to the hospital with left upper quadrant pain radiating to back, associated with nausea but no vomiting. On admission her blood glucose was 472, lipase 11241 and amylase 1227. CT abdomen showed diffusely enlarged pancreas with fat stranding consistent with acute pancreatitis. Ultrasound abdomen did not show any gallstones or biliary dilatation. No history of alcohol abuse or use of estrogens. No family history of hyperlipidemia.

Her blood was grossly lipemic and lipid panel showed triglycerides of 9154. HbA1C was 13.8 and TSH 1.3. She was started on IV fluids receiving a total of 9 liters normal saline. She was given 12 units of lantus subcutaneously with 14 units of insulin aspart. She also received 5000 units of heparin subcutaneously t.i.d. Next morning her pain was much better, lipase decreased to 1797 and triglycerides dropped to 666. She was continued on insulin lantus, aspart and discharged when triglycerides were around 450.

Hypertriglyceridemic pancreatitis has been treated with infusions of insulin and/or heparin, and apharesis to remove triglyderides. Diabetic patients are treated aggressively with IV insulin infusions and heparin, both of which enhance LPL activity. In our case, subcutaneous insulin with subcutaneous heparin resulted in marked improvement in symptoms and lab values.

CAN APRICOT KERNELS FATTY ACIDS DELAY THE ATROPHIED HEPATOCYTES FROM PROGRESSION TO FIBROSIS IN DIMETHYLNITROSAMINE (DMN)-INDUCED LIVER INJURY IN RATS?

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Background and aims:
The present study was aimed to analyze the chemical composition of ground apricot kernel (GAK) and examine its effect on hepatic fibrosis *in vivo* induced by dimethylnitrosamine (DMN) in rats.

Methods and results:
Hepatic fibrosis was induced by intraperitoneal injections of 10 mg/kg DMN for 3 consecutive days each week over a period of 4 wk. The rats were randomly assigned to five groups of nine rats each: the negative control group (NC), the hepatic fibrosis group (PC), hepatic fibrosis supplemented with GAK (0.5 mg/kg/BW/rat), hepatic fibrosis supplemented with GAK (1 mg/kg/BW/rat) and hepatic fibrosis supplemented with GAK (1.5 mg/kg/BW/rat). Rats were killed, blood was collected and livers were excised for biochemical measurements and histological examination. Results indicate that the diet supplemented with GAK led to improving liver function, lipid peroxides, and liver CAT, SOD and GSH. These results were confirmed by liver histology. Hierarchically high levels f GAK (1.5 mg/kg/BW/rat) gave the best results compared to other tested levels.

Conclusion:
This study demonstrates that GAK administration specifically (1.5 mg/kg/BW/rat) can effectively improve liver fibrosis caused by DMN, and may be used as a therapeutic option and preventive measure against hepatic fibrosis. Furthermore, a human trial would be applied specially GAK is a part of Egyptian diet. The act of why high amounts of GAK was improved biochemical values compared to low or moderate levels tested in this study may be due to increase levels of oleic acid and other polyphenols in apricot kernels

Keywords:
Ground apricots kernel (GAK); Antioxidant activity; Cyanide; Dimethylnitrosamine; Liver fibrosis

F-18 FDG PET AS A BIOLOGICAL MAKER FOR SYSTEMIC PLAQUE INSTABILITY: DEMONSTRATION OF PLAQUE INFLAMMATION BY PET

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Background:
A systematic plaque instability is suggested in patients with acute coronary syndrome. Plaque inflammation could be assessed by F-18 fluorodeoxyglucose Positron Emission Tomography (F-18 FDG PET). We investigated whether carotid plaque inflammation could be related to coronary plaque instability using 18F-FDG PET.

Methods:
In 50 (male 14, 48.1±7.7yrs) patients who were newly diagnosed as acute coronary syndrome (28 patients, male 6, 46.87.9 yrs) or stable angina (22 patients, male 13, 49.5±9.8), the co-registration of PET and contrast enhanced computed tomography (CT) images was performed within 1 week after percutaneous coronary intervention. Tthe multislice CT angiogram were acquired at 180 min on the Philips GEMINI TF scanner with 16 slice CT. The maximum standardized uptake values (SUVs) were measured in individual plaques. Results: In all patients, carotid plaque with increased 18F-FDG uptake was observed in the fused PET/CT images. Age and gender-adjusted SUV of FDG on PET scan was significantly higher in the carotid plaques of patients with acute coronary syndrome than those of patients with stable angina (mean 4.13±1.24 (3.19 to 5.27) vs. 2.87±0.98 (2.47 to 3.62), p=0.003). There were no differences of risk factors between two groups.

Conclusions:
The patients presenting with acute coronary syndrome demonstrate simultaneous increase of inflammatory activity of the carotid plaque, supporting a potential causal role of inflammation regarding widespread plaque destabilization associated with acute coronary syndrome.

ATHEROSCLEROTIC PLAQUE INFLAMMATION SYNCHRONIZE WITH INFLAMMATORY ACTIVITY OF VISCERAL FAT

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Background:
Visceral adipose tissue is thought to confer increased cardiovascular risk through leukocyte infiltration and increased adipose macrophage activity. Previous positron emission tomography (PET) studies using fluorodeoxyglucose (FDG) demonstrated that increased FDG uptake could reflect the severity of inflammation in atherosclerotic plaque. We hypothesized that active atherosclerotic change in the major arteries would accompany increased inflammation within visceral fat and it could be detected in humans using combined FDG PET/computed tomography (CT).

Methods:
We observed 44 consecutive subjects with cardiovascular disease. For all of them, an one-hour PET/CT (from brain to foot) was performed after injection of FDG (370-555 MBq). FDG uptake in the aorta or its major branches was evaluated visually and semiquantitatively. Maximal standard uptake values (SUV) of the highest regions of interest were calculated in the subcutaneous fat and visceral fat area, separately.

Results:
Significant FDG uptake in the arterial wall was noted in 21 patients (plaque positive; PP group), all of whom have experienced acute cardiovascular events (acute coronary syndrome or ischemic stroke) within a week. The other 23 patients (plaque negative; PN group) had chronic stable angina or asymptomatic carotid stenosis. Visceral fat SUV was significantly higher as compared to subcutaneous fat SUV (0.49±0.15 vs. 0.15±0.05, p<0.001) in PP group, whereas there was no significant difference in PN group (0.18±0.07 vs. 0.16±0.03, p=0.622). When we compared two groups, PP group showed higher visceral fat SUV than PN group (p<0.001). In terms of subcutaneous fat SUV, the results were similar in two groups (p=0.773).

Conclusions:
We demonstrated that atherosclerotic plaque inflammation was associated with increased inflammation within visceral fat. Our results need to be confirmed by comparison with histologic or other imaging findings. Further evaluation to

determine whether metabolic activity of visceral adipose tissue is a marker or mediator of vascular inflammation is also needed.

PROTECTION AGAINST SPONTANEOUS ONSET OF APOPTOTIC CELL DEATH IN ISOLATED PANCREATIC ISLETS BY LOW-LEVEL-NITRIC OXIDE (NO)/CGMP/PROTEIN KINASE G TYPE-I (PKG-I) SIGNALING PATHWAY, MEASURED BY ULTRASENSITIVE CAPILLARY-ELECTROPHORESIS/LASER-INDUCED-FLUORESCENCE-DETECTOR (CE-LIF) AND NANOPRO (CE-CHEMOLUMINESCENCE/ PROTEIN-IMMUNO-QUANTIFICATION) SYSTEMS

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Our studies have shown that basal or moderately-elevated PKG-I kinase activity is essential for the survival of neural cells (hippocampal neurons, N1E-115, NG108-15 and PC12 cells), primary vascular smooth muscle cells, OP9 bone-marrow stromal cells and human ovarian cancer cells. The present study determines if basal activity of soluble guanylyl cyclase (sGC)/cGMP/PKG-I pathway is necessary to prevent spontaneous apoptosis in mouse primary/ isolated pancreatic islets (model of islet-transplantation therapy). Apoptotic-DNA-fragmentation levels were determined by ultrasensitive-quantitative technique pioneered in our laboratory using CE-LIF technology. The NO-donor S-nitroso-N-acetylpenicillamine (SNAP) caused significant ($P<0.001$) decrease in apoptotic DNA fragmentation at low/physiological concentration (50 M), but increased DNA fragmentation at high/toxic concentration (1000 M), determined by CE-LIF, Cell-Death-Detection-ELISA and TUNEL-staining. The sGC inhibitor ODQ and specific-PKG-I inhibitor DT-2 increased apoptotic DNA fragmentation, indicating essential role of basal PKG-I kinase activity in protecting pancreatic islets. ODQ-induced apoptosis was completely prevented by PKG-I -activating agents that bypass the ODQ block, including atrial natriuretic peptide (ANP, 10 nM) and brain natriuretic peptide (BNP, 100 nM), which activate particulate guanylyl cyclase, or 8-Br-cGMP, direct PKG-I activator. We also used the newly-developed ultrasensitive NanoPro100 system (ProteinSimple, Santa Clara, CA) to show PKG-I expression/phosphorylation levels in isolated pancreatic islets. NanoPro100/1000 system is an automated CE-chemoluminescence/immuno-quantification instrument, which provides exceedingly-high sensitivity (femtogram quantities of protein) and better phospho-protein resolving power, compared with conventional Western blot.The data suggest basal NO/ cGMP/PKG-I activity is essential for preventing spontaneous onset of apoptosis in pancreatic islets after isolation, potentially important for improving outcome of transplantation therapy in diabetic patients.

THE EFFECTS OF COLESEVELAM ALONE OR IN COMBINATION WITH PIOGLITAZONE OR METFORMIN ON PANCREATIC ISLET CELL PROLIFERATION, INSULIN RESISTANCE AND WHOLE-BODY GLYCOLYTIC DISPOSAL OF GLUCOSE IN ZUCKER DIABETIC FATTY RATS

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Introduction:
We investigated the unique and additive mechanism(s) of glucose lowering of colesevelam, pioglitazone and metformin in diabetic ZDF (fa/fa) rats.

Methods:
Eight week old male ZDF (fa/fa) rats were randomized based on HbA1c, glucose and weight to vehicle, colesevelam, pioglitazone, metformin, colesevelam plus pioglitazone or colesevelam plus metformin treatments. Compounds were administered for four weeks as ad-mix to chow. Effect of treatment on islet cell proliferation was measured as the incorporation of deuterium (^2H) from heavy water ($^2HO_2$)into the deoxyribose moiety of pancreatic islet DNA (1). Insulin resistance (IR) and glycolytic disposal of an oral glucose load (glycolysis) were measured with the ^2H-glucose disposal test (2). HbA1c, glucose and insulin concentrations were also measured.

Results:
All treatments improved glucose control to a similar degree. Colesevelam had no effect on insulin resistance (IR) and insulin concentrations but increased glycolysis and islet cell proliferation. Pioglitazone improved IR, decreased insulin concentrations, increased glycolysis and decreased islet cell proliferation. The decrease in proliferation persisted when colesevelam was added to pioglitazone.

Metformin had no effect on IR, insulin concentrations, glycolysis or islet cell proliferation. Adding colesevelam to pioglitazone had an additive effect on the improvement of IR and glycolysis and no additive effects were seen with metformin.

Conclusion:
Colesevelam improves glucose control differently than pioglitazone and metformin by increasing islet cell proliferation and glycolysis without affecting insulin sensitivity. Co-administration of colesevelam and pioglitazone has an additive effect on glycolysis and IR and might be a valuable approach for treating type 2 diabetes.

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TO EVALUATE CORRELATION OF ARTERIAL PRESSURE WITH PULSE WAVE VELOCITY AND OTHER METABOLIC RISK FACTORS IN TYPE 2 DIABETIC POPULATION

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Aim:
To evaluate correlation of arterial pressure with pulse wave velocity and other metabolic risk factors in Type 2 diabetic population.

Methods and Materials:
3700 Type 2 diabetes patients were enrolled in this study. Patients were divided into 3 groups according to their age. Group A - (30-45yrs.) had 759, (499 males/260 females). Group B - (46 – 55 yrs.) had 1123, (697 males / 496 females). Group C - (56 – 65 yrs.) had 627, (364 males/ 263 females). baPWV, Blood Pressure, ABI (ankle-brachial index), HbA1c, Duration of Diabetes, WHR (wait hip ratio), BMI (Body mass Index), Lipids of all the subjects in all age groups were measured.

Results:
Arterial pressure both SBP and DBP has strong correlation with Age,(p - <0.0001) baPWV (p - <0.0001), Duration Of Diabetes (p- < 0.0001) in all age groups. Younger group of patients (group A) had significant correlation with HDL, WHR, BMI (Obesity).

Conclusion:
PWV and Arterial pressure has shown strong correlation in all age groups. Since PWV is a strong future atherosclerotic disease risk marker, regular screening of pulse wave velocity is advisable in all diabetic population in all ages to assess atherosclerosis and future cardiovascular risk.

MACROPHAGE AND T LYMPHOCYTE INFILTRATION IN GLUTEAL VERSUS SUBCUTANEOUS ADIPOSE TISSUE IN OBESE WOMEN

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Aim:
Gluteal adipose tissue (AT) is associated with protective role in obesity and thus, expected to have lower expression of inflammatory markers. However, there are limited data about infiltration of immune cells into gluteal AT in obese patients. Therefore we compared the gene expression of lymphocyte and macrophage markers in abdominal and gluteal subcutaneous AT.

Methods:
14 premenopausal healthy obese women participated in this study. The paired samples of subcutaneous AT were acquired from the abdominal and gluteal region by needle biopsies. Total RNA isolated from AT samples was reverse transcribed to cDNA and preamplified. The mRNA expression of 10 markers was assessed using Biomark Real Time qPCR system and 96x96 chip.

Results:
The expression of 6 among 7 macrophage markers (ACP5, CD68, MSR1, FCGBP, PLA2G7, SPP1) was similar in the two depots. However, gluteal AT had higher expression of lymphocyte markers (RANTES, TCRA, CD3G, TLR 2) (4 from 5) compared to subcutaneous AT.

Conclusions:
Contrary to our hypothesis, the gluteal AT in healthy obese women does not show a lower infiltration of macrophages. Moreover, gluteal AT exerted signs of enhanced accumulation of T lymphocytes; the cells that were shown to precede and initiate macrophage infiltration.

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RENAL HYPERFILTRATION IS ASSOCIATED WITH DECREASED CEREBRAL FLOW RESERVE AND INCREASED STROKE RISK IN PATIENTS WITH METABOLIC SYNDROME OR DIABETES MELLITUS

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Background:
Cerebral flow reserve (FRi) by brain SPECT correlates with increased stroke risk in metabolic syndrome or diabetes mellitus (DM) patients with decreased glomerular filtration (GFR < 60 ml/min-1.73 meter sq) as we previously reported. Findings reported here are for similar patients with renal hyperfiltration (GFR > [140 - A]), where A is age in years.

Methods:
Brain SPECT, basal and perfusion-stimulated with 500 mg acetazolamide IV or 0.8 mg nitroglycerin sublingual, used Tc-99m-HMPAO or Tc-99m-ECD. Activity within computer-defined isocontours defined cortical metabolic and perfusion indices (CMi, CPi) and FRi = CPi – CMi. Test Your Memory (TYM) scores, normal (47+-2), monitored cognition.

Results:
Normal CMi (57.9+-13.4)%, CPi (68.9+-12.4)%, FRi (11.0+-8.1)% were based on 27 low-disease-likelihood patients age (52.4+-16.7) years. In renal hyperfiltration patients (n = 58), age (55.6+-16.1) years, with cognitive complaints, TYM (44.8+-3.4), ($p < 0.001$), 32 (47%) had metabolic syndrome, 20 (34%) had type 2 DM, 1 (1.7% had type 1 DM, 8 (14%) smoked cigarettes, 9 (16%) had stroke and CMi was (54.7+-7.2)%, ($p < 0.01$), CPi (54.6+-7.8)% ($p < 0.0001$) and FRi (-0.1+-15)% ($p < .0001$). Corrected FRi = FRi – [(0.1)(GFR + A) – 14] correlated with stroke risk with GFR in ml/min, cf. prior correction term [9 – 0.1(GFR)], with GFR in ml/min-1.73 meter sq, for patients with renal insufficiency.

Conclusions:
Renal insufficiency and renal hyperfiltration are both directly related to decreased cerebral flow reserve (corrected FRi from brain SPECT) and increased stroke risk in mildly cognitively impaired diabetic or insulin resistant patients.