

ABSTRACTS

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A CORRELATIONAL STUDY ON PLASMA RESISTIN LEVELS AS A BIOCHEMICAL INDICATOR FOR DIABETIC NEPHROPATHY AND OTHER MICROANGIOPATHIES IN TYPE 2 DIABETIC PATIENTS

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Resistin is an adipocyte-secreted peptide. The relationship between circulating resistin concentrations and various pathophysiological aspects of type 2 diabetes mellitus, if any, remains poorly understood. In human studies, relationships of circulating resistin to indicators of insulin sensitivity, adiposity and type 2 diabetes have been inconsistent and controversial. This study investigated the importance of resistin as a biochemical indicator of clinical complications in male and female patients with type 2 diabetes mellitus. Fasting resistin plasma levels were measured in a total of 140 male and female type 2 diabetic patients. The correlation of determined resistin levels in type 2 diabetic patients with the following clinical complications: diabetic nephropathy, diabetic retinopathy, peripheral neuropathy were investigated. This study revealed that the mean plasma resistin level was significantly higher ($P = 0.001$) by 51% in nephropathy-positive group (10.76 ng/ml) compared to nephropathy-negative group (7.12 ng/ml). Moreover, it was also found that the mean plasma resistin level was significantly higher ($P = 0.001$) by 33% in neuropathy-positive group (9.47 ng/ml) compared to neuropathy-negative group (7.11 ng/ml). No statistically significant difference in mean plasma resistin levels was found in retinopathy-positive group (8.40 ng/ml) compared to retinopathy-negative group (7.63 ng/ml).

The results of this investigation may help to elucidate the role of resistin in the pathogenesis of diabetic complications and will facilitate its utilization in the prediction and prevention of these clinical complications.

INDIA IS THE ERECTILE DYSFUNCTION CAPITAL OF THE WORLD

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Introduction: According to IDF (International Diabetes Federation) There are 382 Million Diabetics across the globe. One third of these Diabetics are in India, closely competing with China. So India is the Diabetes Capital of the world. The Commonest complication of Diabetes

in Men is Erectile Dysfunction. So India is the Erectile Dysfunction Capital of the world.

Objectives: Since Erectile Dysfunction is the Earliest Marker of Myocardial ischaemia. Our aim is to study the prevalence of Erectile Dysfunction and detect it as early as possible in every Diabetic and promote measures to provide them adequate education, lifestyle modification and necessary medical therapy to retard the onset of critical ailments like MI or Stroke in these subjects.

Methods: 54,362 patients, all diabetics, were studied, Complete detailed medical history and Sexual history was taken, Basic Investigations like BI Sugars Fasting PP, Hba1C, Lipid Profile, Renal Functions, Liver Functions, Uric Acid, Vit D, Serum Testosterone, Free and Total, SHBG, Serum PSA Free and Total, Thyroid studies, Urine routine were done. Besides this we also did their dental examination, Digital Rectal examinations, USG of Scrotum and Penile Doppler studies and sleep studies. We also did the Resting ECG and Coronary Angiogram. We also did the IIEF Scores and B Depression Scores. We gave questionnaire to 800 GPs to follow up the diabetic patients with ED after the onset of diagnosis for symptoms CAD.

Results: Over 70 percent of Male Diabetics had ED at Diagnosis. 9 years follow done and 84 percent had signs and symptoms suggestive of CAD. In Women diabetics Hypoactive Sexual Desire disorders and Depression. We compared all these results with data from China and other countries.

Conclusions: India ranks highest in the prevalence of Diabetes. in men ED is commonest complication, hence India is Erectile Dysfunction capital of the world.

EXTRACELLULAR FATTY ACID SYNTHASE (FASN) AS A NOVEL BIOMARKER OF OBESITY-INDUCED INSULIN RESISTANCE AND METABOLIC SYNDROME

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Objective: The objective of this study was to evaluate whether circulating FASN could be a novel biomarker associated with measures of insulin resistance and presence of metabolic syndrome in obese individuals.

Methods: The study was carried out on three different groups of subjects: G1: twenty obese adult individuals with metabolic syndrome. G2: twenty age-matched obese adults

without metabolic syndrome. G3 (Control G): twenty age-matched non obese healthy adult volunteers. Both group (1) and (2) were chosen to be obese (Body Mass Index (BMI) is greater than 30 kg/m²). Age of subjects in all groups: 20-60 years. All were subjected to: complete physical examination, assessment of criteria of metabolic syndrome according to the National Heart, Lung, and Blood Institute (NHLBI) and the American Heart Association (AHA), fasting plasma glucose (FPG), fasting insulin, lipid profile, assessment of insulin resistance by HOMA-IR and measurement of plasma FASN level using ELISA technique.

Results: the plasma FASN levels were significantly increased in G1 than other two groups (median 19.95 ng/ml for G1 vs 7.7 and 7.9 ng/ml for G2 and G3 respectively, $P < 0.001$). Evident positive correlations were found between plasma FASN level and HOMA-IR, FPG, TG, WC and BMI and negative correlation with HDL level ($P < 0.05$ for HOMA-IR and FPG; $P < 0.01$ for TG, WC, BMI and HDL). The area under the receiver-operating characteristic curve (AUC) for FASN was 0.92 (95% confidence interval, CI: 0.84 to 0.99) but was not significantly different from 0.86 (95% CI: 0.75 to 0.96) for HOMA-IR.

Conclusion: Our results suggest that circulating FASN is a biomarker of obesity-induced insulin resistance that could provide diagnostic advantage to measures of metabolic syndrome.

ALTERATION OF ADIPOKINES AND PULMONARY FUNCTION IN OBESE ASTHMATIC ADOLESCENTS

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Introduction: Obesity and asthma prevalence have been increasing over the past decade. Obesity is an independent risk for asthma. Obesity-associated asthma has been proposed to be a distinct entity. The mechanistic basis for these associations in humans is not established, although a possible role for adipokines has been invoked.

Objectives: The aim of this study was to evaluate serum levels of leptin, high-molecular-weight (HMW) adiponectin, and retinol-binding protein 4 (RBP4) in obese and non-obese children with or without asthma and in healthy non-asthmatic Mexican adolescents, and analyze their relationships with lung function.

Methods: This study enrolled 195 Mexican adolescents in 4 study groups: non-obese non-asthmatics (n = 63), non-

obese asthmatics (n = 58), obese non-asthmatics (n = 46) and obese asthmatics (n = 28). All underwent pulmonary function testing. Blood was collected for measurement of serum adipokines.

Results: Obese non-asthmatics and obese asthmatics had significantly higher levels of leptin and lower levels of HMW adiponectin compared to non-obese asthmatics and non-obese non-asthmatics. Subjects with asthma had higher levels of RBP4 compared to the adolescents without asthma independent of the presence or absence of obesity. The level of HMW adiponectin was negatively correlated with forced expiratory lung volume in the first second (FEV1) and forced vital capacity (FVC) in all studied subjects. Obese asthmatics had lower FEV1/FVC ($P = 0.034$) compared to the non-obese non-asthmatics subjects. **Conclusions:** Our study suggests that obesity-associated asthma is indeed a distinct entity from asthma in the non-obesity in adolescents. Moreover, the direct association of adipokines with pulmonary function suggests that interventions addressing onset and progression of obesity may have the most substantial impact on decreasing the morbidity occurring with obesity-associated asthma. (HIM/2013/015)

Keywords: obesity; asthma; adipokines; pulmonary function

ROLE OF ORAL CHOLECALCIFEROL AS ADJUVANT THERAPY IN TYPE 1 DIABETES MELLITUS: RANDOMIZED CONTROLLED TRIAL

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Introduction: The vitamin D hormone system has been implicated in the pathogenesis of several autoimmune diseases, including Type 1 Diabetes Mellitus, as an adaptive immune system modulator.

Objectives: The objective of this study is to examine the role of cholecalciferol in modulating the altered immune response in T1DM, thereby improving glycemic control and residual pancreatic Beta-cell function, measured objectively by Hemoglobin A1c levels, GAD65 antibody titers and C-peptide levels.

Method: 52 T1DM patients aged 1-18 years attending JIPMER Pediatrics department in year 2014 were randomized into two groups. High dose oral cholecalciferol therapy (1.2 lakh IU per month) was instituted in addition

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to insulin in intervention arm, while only insulin was continued in other arm for 6 months.

Results: Prevalence of Vitamin D deficiency was as high as 63.5% among T1DM patients in our study. The Cholecalciferol group achieved significantly lower HbA1c levels at 3 and 6 months follow-up than controls ($P<0.05$). The mean C-peptide levels were significantly greater ($P<0.05$) in cholecalciferol group as compared to controls at end of 6 months. Median difference in GAD65 antibody levels was not significant between the groups at the end of 6 months. No adverse events due to cholecalciferol therapy were reported.

Conclusions: Our study shows that high dose oral Cholecalciferol concomitant with insulin therapy is safe and is related to slow decline of residual β -cell function in T1DM patients, thereby enhancing glycemic control. An affordable, safe and easily obtainable vitamin may serve as a novel approach in the fight against a costly, debilitating, chronic disease.

Clarification: Higher C-peptide shown in the cholecalciferol group could be mediated by its direct action on B-cell function, increasing the levels of cytosolic calcium that is important for the movement of insulin granules and insulin secretion. Our study highlights the possible protective effect of Vitamin D on Beta-cell function in the pancreas, thereby leading to better glycemic control.

Keywords: *Cholecalciferol; Diabetes Mellitus; Hemoglobin A1c; C-Peptide; Gad65*

EFFECT OF HEPATITIS C VIRUS INFECTION ON METABOLIC AND CARDIOVASCULAR RISK PROFILES OF DIABETIC PATIENTS

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Aims: The aims of this study were to: 1.) Determine the prevalence of Hepatitis C virus infection in diabetic patients. 2.) Elucidate the presence of an association between diabetes and hepatitis by comparing prevalence in diabetics with controls. 3.) Determine the effect of Hepatitis C virus infection on metabolic and cardiovascular risk profiles of diabetic patients.

Methods: Five hundred and fifty diabetic patients attending diabetes clinic were enrolled in the study. Patients' data was collected after taking consent. A control group comprising of 550 healthy blood donors who donated blood

in blood bank of hospital during the study period were taken as controls. Hepatitis C virus antibody presence was checked using ELISA in both control and study group. Patients' glycemic control was checked and lipid profile was analyzed. Blood pressure, body mass index (BMI) and waist-hip ratio (WHR) were measured. All the ethical requirements were met before starting the study. Results: The age of patients was 47.58 years and the duration of diabetes was 7.02 years. Out of 550 patients included in study, 304 were female, 428 were from urban locality and 143 had a positive family history of diabetes mellitus. HCV infection was present in 160 (29.09%) diabetic patients as compared to control in whom prevalence was 8.18% (OR = 4.60, 95% CI = 3.22-6.57, $P<0.01$). Patients with HCV infection had significantly lower total serum cholesterol, serum triglycerides, LDL cholesterol, LDL cholesterol/HDL cholesterol ratio and a lower waist to hip ratio as compared to diabetic patients without HCV infection. In contrast, they had significantly higher random blood sugar value. Furthermore, diabetic patients with HCV infection had insignificantly lower HDL cholesterol, fasting blood glucose and HbA1c level. They also had insignificantly higher systolic blood pressure diastolic blood pressure and BMI when compared with diabetic patients who tested negative for HCV infection.

Conclusion: The study shows that there is a possible association between HCV infection and diabetes. Although HCV infection is associated with high random blood sugar values, the remaining metabolic and cardiovascular risk indicators show a favorable pattern. It is an intriguing finding as HCV infection has been shown to induce insulin resistance compounding diabetes course but in this case, it had a positive influence on the metabolic and cardiovascular risk profiles of diabetic patients

RELATIONSHIP OF GLYCEMIC CONTROL WITH DEPRESSIVE SYMPTOMS IN DIABETES MELLITUS

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Objective: The objective of this study was to assess the effect of glycemic control on the prevalence of depression in diabetes patients and to identify the factors associated with depression in patients with poor glycemic control.

Methods: This study was conducted on a sample of 108 diabetic patients visiting Diabetic Clinic at Nishtar Medical College Hospital, Multan. Laboratory data was used to evaluate glycemic control in patients. Patients were divided into 2 groups on the basis of glycemic control using

HbA1c levels of 7%. Presence of depression was assessed using Aga Khan University Anxiety and Depression Scale (AKUADS) with a cutoff score of 20.

Results: The mean age of patients was 49.32 ± 13.29 years. Using AKUADS, prevalence of depression in diabetic patients was found out to be 59.26%. Twenty five out of the 54 patients with good glycemic control had anxiety and depression while 39 of the patients with poor glycemic control had anxiety and depression. The patients with poor glycemic control were found to be significantly more depressed as compared to those with good glycemic control (OR = 3.02, 95% CI = 1.36-6.73, $P = 0.0034$). Factors found to be associated with the presence of depression in group with poor glycemic control were type of diabetes (OR = 5.83, 95% CI = 1.35-25.13, $P = 0.02$) and marital status (OR = 0.07, 95% CI = 0.07-1.04, $P = 0.05$).

Conclusions: Poor glycemic control was found to be associated with higher likelihood of presence of depression in patients. There is need of early recognition and treatment of this comorbidity in this high risk group as it may improve diabetes outcome.

SELF-MANAGEMENT PRACTICES AND BEHAVIOR OF PAKISTANI PATIENTS WITH TYPE 2 DIABETES

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Objective: The objective of this study was to analyze the self-care practices and behavior of Pakistani patients with type 2 diabetes.

Methods: A random sample of 174 patients was selected for accrual in the study from the diabetic clinic of Nishtar Medical College Hospital Multan. Patients were interviewed using a structured questionnaire to elicit information about their self-management practices and behaviors.

Results: The majority of patients (93.8%) regarded diabetes as a life long illness which patients can control to live a normal life. Most of the patients (96.9%) of the patients recognized the importance of self-management in the control of diabetes. Compliance with medication was reported by 95.5% of the patients, regular exercise was performed by 65.2% patients, dietary modification was practiced by 62.0% patients, and weight control was exhibited by

56.06% respondents while self-monitoring of blood glucose was done by 74.2% of the individuals enrolled in the study. Follow up frequencies of the study participants was 1.63 ± 0.63 visits per month. Self-reported barriers to optimal self-care included cost and access to healthcare, social factors, other health conditions and family problems.

Conclusion: The results of this study show the challenges in improving the control of diabetes in developing countries. Studies are needed to explore the factors affecting self-care practices of diabetic patients.

SERUM CHOLESTEROL LEVELS IN NORMOTENSIVE AND HYPERTENSIVE INDIVIDUALS WITH DIABETES MELLITUS

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Aim: The aim of this study was to: 1.) Evaluate serum cholesterol levels in diabetic patients 2.) Compare the serum cholesterol levels in hypertensive and normotensive diabetes mellitus patients.

Methods: A comparative study was done on 230 diabetes patients seen at diabetes clinic at Nishtar Hospital, Multan between 1st July and 30th August, 2008. Patients were divided into normotensive, prehypertensive and hypertensive on the basis of blood pressure and their cholesterol levels were compared. Data was analysed using SPSS v.16.

Results: The mean age of patients was 46.25 ± 11.28 years while the mean duration of diabetes was 78.36 ± 66.90 months. Serum cholesterol levels in patients were 187.75 ± 38.53 mg/dl. Serum cholesterol levels in hypertension patients (192.75 ± 38.25 mg/dl) were significantly higher than patients whose blood pressure was in normal age (164.75 ± 23.75 mg/dl) Prehypertension patients had levels of cholesterol (181.5 ± 38.5 mg/dl) in between those of normotensive and hypertensive patients.

Conclusion: Increasing levels of serum cholesterol with increasing blood pressure show that hypertensive diabetes mellitus patients are at high risk of atherosclerosis. Aggressive control of diabetes as well as medication and lifestyle changes are required to prevent progression of complications associated with atherosclerosis resulting in decreased morbidity and mortality.

EVALUATION OF LIVER FUNCTION TESTS IN TYPE 2 DIABETIC PATIENTS: EXPERIENCE FROM NORTHERN BANGLADESH

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Objectives: To find out the liver dysfunction in type 2 diabetes mellitus as evidenced by liver function tests and the extent and severity of abnormalities of liver function tests.

Methods: It was a descriptive cross-sectional comparative study carried out in Department of Medicine, Rajshahi Medical College Hospital and Rajshahi Diabetic Association Hospital from July, 2012 to June, 2014. 100 (one hundred) diagnosed type 2 diabetic patients and 30 apparently healthy people. All of those study population were free from taking any hepatotoxic drugs and free from any preexisting liver disease. This exclusion was done by history, through clinical examination and relevant investigations.

Results: The prevalence of abnormal serum bilirubin, ALT, AST, Alkaline phosphatase, prothrombin time and S. albumin were 6%, 30%, 7%, 6%, 54% and 12% respectively in type 2 diabetic patients and 00%, 3.3%, 00%, 6.7%, 10% and 3.3% respectively in normal people. All the LFTs of type 2 diabetic patients were mildly abnormal except 2 patients (2%) had moderate elevation of ALT, 7 patient (7%) had markedly prolonged PT, and 1 patient (1%) had moderately decreased s. albumin. In normal people all LFTs abnormalities were mild.

Conclusion: A high proportion of patients with type 2 diabetes mellitus in our country have abnormal liver function tests that may be a marker of NAFLD and insulin resistance, such patients would thus warrant more intensive glycaemic control to prevent progression of significant liver diseases.

NARINGIN MITIGATES CARDIAC HYPERTROPHY AND OXIDATIVE STRESS ASSOCIATED JNK ACTIVATION IN TYPE 1 DIABETES

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Cardiac hypertrophy in type 1 diabetes mellitus is attributed to increased oxidative stress associated activation of c-Jun Nuclear Kinase (JNK). We investigated the effects of naringin on hyperglycemia-associated oxidative stress, activation of JNK-1 and cardiac hypertrophy. Male

Sprague-Dawley rats (225-250 g) (n = 7) were divided into 6 groups. Groups I and II were orally treated with distilled water {3.0 ml/kg bodyweight/day (BW)} and naringin (50 mg/kg BW), respectively. Groups III-VI were rendered diabetic by a single i.p injection of 60 mg/kg BW of streptozotocin (STZ). Groups III, IV, V and VI were further treated with subcutaneous insulin (4.0 I.U, twice daily), naringin (50 mg/kg BW), distilled water (3.0 ml/kg) and ramipril (3.0 mg/kg BW), respectively. After 56 days, the animals were sacrificed then plasma and cardiac tissues obtained for further analysis. Naringin treatment of diabetic rats significantly reversed oxidative stress, lipid peroxidation, proteins oxidation, cardiac hypertrophy indices, and JNK protein activation compared to untreated diabetic animals. Our results do suggest that naringin mitigates cardiac hypertrophy by inhibiting oxidative stress leading to inactivation of JNK-1. Naringin supplements could therefore ameliorate cardiac hypertrophy in diabetic patients.

EVALUATION OF METABOLIC SYNDROME AND ESCALATION OF CARDIOVASCULAR EVENTS IN ASIAN INDIAN TYPE 2 DIABETIC SUBJECTS

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The present study aimed at estimating the prevalence of metabolic syndrome (MetS) and evaluating the escalation of cardiovascular risk factors in Asian Indian type 2 diabetic subjects. A total of 1522 type 2 diabetic subjects aged 25-91 years were screened for hypertension, dyslipidemia, obesity and cardiovascular events. Anthropometric, clinical and biochemical measurements were done in all subjects. The prevalence of MetS was estimated in all the subjects according to the new harmonized criteria of 2009. The prevalence of MetS among urban Indian diabetic subjects was 71.9% and was significantly higher in females (86%) as compared to males (57.9%). MetS subjects had higher values of BMI, waist and hip circumferences, WHR, SBP, DBP, glucose, cholesterol, Triglycerides, while low level of HDL-cholesterol. To determine the independent predictors of the MetS in diabetic sample, binary logistic regression analyses were performed using demographic and biochemical parameters. Significant differences in the indices of generalized and abdominal obesity and lipids were observed ($P < 0.01$) in male: female and MetS and non-MetS comparisons. Regression analysis for prediction of cardiovascular disease (CVD) shows that family history of diabetes, age, BMI, physical inactivity and hypertension independently and significantly predicted the disease outcome. In conclusion, this study demonstrated the high prevalence of MetS and its different components were positively as-

sociated with a higher risk of CVD in north Indian diabetic population. Nevertheless, MetS is a major health problem in India, comprehensive population studies are warranted for estimation of incidence and prevalence, and education should be provided on its prevention and control to reduce the diabetes-related morbidity and mortality.

HYDROXYTYROSOL: POTENTIAL AS AN ATHEROSCLEROSIS THERAPEUTIC

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Objectives: To delineate the roles of the olive oil-derived anti-oxidant, hydroxytyrosol, in key processes initiated by endothelial dysfunction during atherosclerosis.

Background: Cardiovascular disease accounts for 31.9% deaths in the US. Arterial inflammation and high cholesterol burden promote atherosclerosis, increasing the risk of heart attack and stroke. Statins offer the most promising therapeutic by inhibiting *de novo* cholesterol synthesis, however, only account for 30% reductions in major cardiovascular events. The olive oil-rich diet has long shown correlation with reduced cardiovascular events and reduced serum LDL, implicating components of olive oil as potential atherosclerosis therapeutics. Hydroxytyrosol, a major polyphenol of olive oil, is a promising therapeutic; however, its action and underlying mechanisms during atherosclerosis are poorly understood.

Methods and Results: Endothelial dysfunction in atherosclerosis leads to chemokine-mediated recruitment of monocytes. This process can be recapitulated *in vitro* using a Boyden chamber. Hydroxytyrosol, at various concentrations, significantly attenuated the chemokine-driven monocytic migration in such assays. Additionally, hydroxytyrosol inhibited the peroxide-induced production of reactive oxygen species in both human monocytes and macrophages. The expression of pro-inflammatory genes (e.g. MCP-1 and ICAM-1) was also significantly reduced in human macrophages. Hydroxytyrosol also significantly stimulated radioactive cholesterol efflux from foam cells of human macrophages. This correlated with increased expression of genes implicated in this process. Western blot analysis using phospho-specific antibodies showed an important role of STAT1 Ser⁷²⁷ phosphorylation in the actions of hydroxytyrosol in human macrophages.

Conclusions: These data demonstrate beneficial effects of hydroxytyrosol in reducing key hallmark events associated with endothelial dysfunction and atherosclerosis initiation.

CORRELATION OF MICROALBUMINURIA WITH OBESITY AND CARDIOVASCULAR RISK MARKERS IN TYPE-II DIABETIC NORTH INDIAN PUNJABI POPULATION

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Carewell Heart & SuperSpeciality Hospital

Background and Aims: Microalbuminuria has been identified as a predictor of renal failure and an independent risk factor for cardiovascular disease in patients with diabetes mellitus as well as in general population. This study was aimed to determine the correlation of microalbuminuria with Obesity and Cardiovascular risk markers.

Methods and Materials: 2044 Type II diabetes patients were enrolled in the study. Microalbuminuria in all the subjects was estimated and the albumin to creatinine ratio (A:C) determined. Obesity parameters (BMI, WHR), HbA1c, baPWV, Blood Pressure, ABI, LDL, HDL, TGs of all the subjects were also measured. baPWV was measured with VP-2000/1000-Colin Corporation, (hyayashi komaki Japan). Microalbuminuria was measured Clinitek status Analyzer. (Bayer Health Care).

Results: Overall prevalence of microalbuminuria was 58.4% (54.6% M/64.2%F). Microalbuminuria had a highly significant correlation with duration of diabetes ($P<0.001$), HbA1c and BMI ($P<0.05$), Systolic and diastolic blood pressure ($P<0.01$). Positive correlation was found with PWV, ABI, Cholesterol, LDL & TG.

Discussion: The high proportion of type 2 diabetes patients with microalbuminuria raises implications for health policy in North India. Screening programs and optimized control of modifiable risk factors are needed to reduce the risk of diabetic nephropathy.

BODY-MASS INDEX, WAIST-SIZE, WAIST-HIP RATIO AND CARDIOVASCULAR RISK FACTORS IN NORTH INDIAN PUNJABI DIABETIC POPULATION

Rohit Kapoor

Carewell Heart & SuperSpeciality Hospital

Objective: To determine the association of obesity, measured by body-mass index (BMI), waist-size or waist-hip ratio (WHR), with multiple risk factors in Punjabi population. **Methods:** 2015 (1157 M, 858 F) T2D subjects, aged between 31-79 yrs were enrolled for the study. Waist Hip Ratio (WHR), Waist Circumference (WC), Body Mass In-

dex (BMI), Systolic Blood Pressure(SBP), Diastolic Blood Pressure (DBP), Lipid Profile (Total Cholesterol, Triglycerides, HDL, LDL), Pulse Wave Velocity (baPWV), **Ankle brachial index** (ABI) and HbA1c of the subjects were analyzed. Pearson's correlation coefficients (r) of BMI, waist and WHR with various risk factors were determined.

Results: There is a positive correlation of BMI, waist-size and WHR with SBP ($r = 0.18$ to 0.07), DBP (0.13 to 0.08), duration of diabetes ($r = 0.10$ to 0.07), HbA1C ($r = 0.126$ to 0.08), Total cholesterol (0.23 to 0.09), and LDL cholesterol (0.12 to 0.07) and negative correlation with HDL cholesterol ($r = -0.11$ to -0.08) in both men and women ($P < 0.05$). Triglycerides were found to be significantly correlated with BMI and WHR only ($P < 0.05$). No significant correlation was found with PWV & ABI.

Conclusion: There is a positive relationship of markers of obesity (body-mass index, waist size and waist hip ratio) with major cardiovascular risk factors and regular anthropometric measurements are needed in diabetic population to prevent future CV risk.

OVERALL AND ABDOMINAL ADIPOSITY AND HYPERTRIGLYCERIDEMIA AMONG NORTH INDIAN PUNJABI DIABETIC POPULATION

Rohit Kapoor

Carewell Heart & SuperSpeciality Hospital

Objective: To determine the association of obesity, measured by body-mass index (BMI), waist-size or waist-hip ratio (WHR), with hypertriglyceridemia in North Indian Punjabi diabetic population.

Methods: 2015 (1157 M, 858 F) T2D subjects, aged between 31-79 yrs were enrolled for the study. Waist Hip Ratio (WHR), Waist Circumference (WC), Body Mass Index (BMI) and Triglycerides of the subjects were analyzed. Results: The mean age of the subjects was 52.9 yrs (5.09). The mean BMI of subjects was 26.5 (4.4), WHR 1.1(0.02) and WC 39.7 (4.1) inches. There is a positive correlation of waist circumference ($r = 0.01$) with triglycerides. There was a significant positive correlation of BMI ($r = 0.08$ M $r = 0.18$ F) and WHR ($r = 0.07$ M $r = 0.07$ F) with triglycerides ($P < 0.05$).

Conclusions: Both BMI and WHR were strongly independently associated with hypertriglyceridemia among the population. Both measurements should be considered for use in assessing health risk at clinical settings and epidemiologic research among diabetic population.

HYPERTENSION AND SUB CLINICAL ATHEROSCLEROSIS THEIR CORRELATION WITH METABOLIC RISK FACTORS IN DIABTIC PATIENTS BY AGE

Rohit Kapoor

Carewell Heart & SuperSpeciality Hospital

Aim: To evaluate correlation of hypertension 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 - (30-45 yrs.) 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 (pulse wave velocity), Blood Pressure, ABI (ankle-brachial index), HbA1c, Duration of Diabetes, WHR (waist hip ratio), BMI (Body mass Index), Lipids of all the subjects in all age groups were measured.

Results: 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 hypertension 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 hypertensive diabetic population in all ages to assess atherosclerosis and prevent future cardiovascular risk.

CORRELATION OF BODY FAT PERCENTAGE TO VARIOUS METABOLIC AND CARDIOVASCULAR RISK MARKERS IN NORTH INDIAN TYPE II DIABETIC PATIENTS

Dr. Rohit Kapoor

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Aim: To determine the association of body fat percentage to various metabolic and cardiovascular risk markers in North Indian type II diabetic patients. METHODS: 1700 (902 M, 798 F) T2D subjects, aged between 31-79 yrs were enrolled for the study. Waist Hip Ratio (WHR), Waist Circumference (WC), Body Mass Index (BMI), Systolic Blood Pressure(SBP), Diastolic Blood Pressure (DBP),

Lipid Profile (Total Cholesterol, Triglycerides, HDL, LDL), Pulse Wave Velocity (baPWV), Ankle brachial (ABI) and HbA1c of the subjects were analyzed. Pearson's correlation coefficients (r) of body fat percentage with various metabolic risk factors were determined.

Results: There is a significant positive correlation of body fat percentage with duration of diabetes, HbA1C, Total cholesterol, Triglyceride, LDL cholesterol, DBP, BMI and WHR and negative correlation with HDL cholesterol in both men and women ($P < 0.05$). No significant correlation was found with SBP, PWV & ABI.

Conclusion: Body fat percentage carries good relationship with major cardiovascular risk factors and regular anthropometric measurements are needed in diabetic population to prevent future CV risk.

SEX SPECIFIC ASSOCIATION AND PREVALENCE OF INSULIN RESISTANCE (HOMA-IR) IN INDIAN DIABETIC POPULATION

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Objective: Determine the prevalence of IR in Indian diabetic population and its correlation with gender and other metabolic factors.

Method: 250 subjects (131 M/109 F), between the age of 26–78 years were recruited for the study. After a 12-hour fasting, blood sample was drawn for biochemical measurements including plasma glucose, insulin and lipids. BMI, waist and hip circumference were also measured. IR was assessed according to HOMA (Mathew et al method) and HOMA- IR > 3.98 was used as IR.

Results: The mean \pm SD age of the sample population was 51.0 ± 11.7 yrs (51.3 ± 11.6 yrs males & 50.8 ± 11.9 yrs females). The BMI (24.8 kg/m^2 males, 22.7 kg/m^2 females), mean FPI (14.9 ± 19.0 males & 12.5 ± 9.2 females) and over all HOMA - IR (4.9 ± 7.3 males & 4.2 ± 3.8 females) was found to be higher in males than females. The prevalence of IR using HOMA - IR estimated was found to be 33.75% (34.35% males and 33.02% females). No significant correlation was found between HOMA - IR and Age, BMI, BP, Lipid profile in both the genders. But in males the correlation of HOMA-IR with FPG ($P = 0.001$),

WC ($P = 0.013$) and HC (0.019) was significant. In females, HOMA-IR was significantly correlated with FPG ($P = < 0.0001$). FPI was significantly correlated with HOMA - IR in the both genders ($P < 0.0001$).

Conclusion: The study concludes that IR is relatively common in male and has correlation with obesity and FPG. Risk factors for IR should be detected in diabetics for effective preventive measures.

SEX AND AGE SPECIFIC ASSOCIATION AND PREVALENCE OF HYPERTENSION IN OVERWEIGHT AND OBESE NORTH INDIAN DIABETIC POPULATION

Dr. Rohit Kapoor

Carewell Heart & SuperSpeciality Hospital

Aim: To determine the prevalence of Hypertension in Overweight and Obese Type 2 diabetic patients and its correlation with age and gender.

Method: 2644 Type 2 DM subjects, aged between 20 – 80 yrs. were enrolled for this study which is a cross-sectional and co- relational study.

Results: From total sample of 2644 subjects with T2DM, 52.83% were overweight and 35.39% obese. There was an increase in prevalence of overweight in male patients, whereas women had an increase in prevalence of obesity. According to BMI, it was noted that there is an increase in prevalence of overweight and obesity grade - II in subjects between the age group of 51- 60 yrs., while obesity grade I & III in subjects from 41-50 yrs. age group. SBP was elevated in 70% in overweight and obese subjects. SBP is slightly high in male but there is no significant difference between genders ($P = 0.84$). Regarding elevated DBP, it affects 35.4% subjects, presenting a greater proportion in males with 42.2% compared to 36.3% females. DBP has a highly significant association with respect to male gender ($P = 0.009$). DBP affects a greater proportion of subjects ranging from 51- 60 yrs.

Conclusion: 52.8% of subjects with overweight and obese suffered from hypertension. High SBP has a greater impact in male patients regardless of age. DBP is statistically significantly higher in males, specifically when they are in between 51- 60 yrs.

SUBCLINICAL ATHEROSCLEROSIS & LEFT VENTRICULAR DIASTOLIC DYSFUNCTION- THEIR CORRELATION IN INDIAN T2DM PATIENTS

Dr. Rohit Kapoor

Carewell Heart & SuperSpeciality Hospital

Aim: To assess the correlation of LVDD with CIMT (carotid intima media thickness) and baPWV - the subclinical atherosclerotic risk markers.

Methods: 565 with diabetes mellitus, aged between 35-75 years were evaluated for left LVDD using Doppler Echo. LVDD was determined by using conventional 2-Decho and Doppler techniques & LVDD was graded as grade I, II, III & IV as per standard norms. Parameters such as CIMT, baPWV, ABI, SBP, DBP, Lipid Profile, HbA1c, Duration of diabetes, WHR were included. LVEF was considered as a measure of systolic dysfunction.

Results: LVDD was observed in 84.6% of patients. Predominant pattern was abnormal relaxation (58%) with highest in age group of 35 -73 yrs. Out of 565 patients studied, total 478 (84.6%) had LVDD, 347 patients (69.4%) had (Grade 1 DD), 104 patients (20.8%) had (Grade 2-), 27 patients (5.4%) had (Grade 3). 87 out (15.4%) had no evidence of diastolic dysfunction. LVDD was found to have significant correlation with SBP ($P = 0.015$), ABI ($P = 0.034$), LDL ($P = 0.06$), HDL ($P = 0.07$) and TG's ($P = 0.18$). Correlation of LVDD with PWV & CIMT is found to be mild significant.

Conclusion: LVDD had mild correlation with CIMT & PWV in this group of population. Since both CIMT & PWV are future cardiovascular risk markers, such correlation warrants screening of diabetic population for these atherosclerotic risk markers for prevention of future cardiovascular risk. However, larger study is needed to observe more correlation between these parameters.

SEX SPECIFIC ASSOCIATION AND PREVALENCE OF METABOLIC SYNDROME IN TYPE 2 DIABETIC SUBJECTS OF NORTH-INDIAN POPULATION

Dr. Rohit Kapoor

Carewell Heart & SuperSpeciality Hospital

Aim: We have examined the prevalence and association of metabolic syndrome clustering among male (aged 58-85 years) and female (aged 55-77 years) Punjabi population.

Methods: This cross-sectional study was carried out on total of 301 (186 males and 115 females) type 2 diabetic mellitus subjects. The risk factors to assess the metabolic syndrome were included body mass index (BMI), waist circumference (WC), high density lipoprotein (HDL), triglycerides (TG), fasting blood glucose (FBS), systolic blood pressure (SBP), diastolic blood pressure (DBP) and to determine the cut-off points of these risk factors for Asian Indians used National Cholesterol Education Program (NCEP) - ATP III and International Diabetes Federation (IDF) criteria. The cut-off points were determined for WC >90 cm in males and >80 cm in females, BMI >23 kg/m² and impaired fasting glucose (IGF) >100 mg/dl.

Results: It was observed that overall type 2 diabetic males (49%) were at risk of developing metabolic syndrome as compared to females (31%). The risk factors of metabolic syndrome such as BMI (34.6% for males and 70.4% for females), SBP (58.8% for males, 53% for females), DBP (38.4% for male, 30.4% for females) and triglycerides (85.48% for males, 85.2% for females) consistently higher in males as compared to females in which waist circumference (75.1% for males, 89.6% for females), HDL (65.9% for males and 89.6% for females) and FBS (64.9% for males and 72.9% for females) were higher. However, the overall mean differences between males and females of all studied risk factors were not found to be statistically significant ($P < 0.05$).

Conclusion: The risk of metabolic syndrome is observed more in type 2 diabetic male Punjabi population due to sedentary lifestyle as compared to female.

PREVALENCE OF PERIPHERAL ARTERIAL DISEASE (PAD) BY MEANS OF ABI IN ASYMPTOMATIC TYPE II NORTH INDIAN DIABETICS AND ITS CORRELATION WITH CARDIOVASCULAR RISK MARKERS

Dr. Rohit Kapoor

Carewell Heart & SuperSpeciality Hospital

Aims: To evaluate the prevalence of PAD by means of ankle-brachial index (ABI) in T2DM patients.-stage I grade 0 category 0 (Fontaine's stages & Rutherford categories classification of PAD) in North Indian population.

Methods: Between winter 2012 & summer 2014, 2778 asymptomatic (no complaints pertaining to PAD) Type II Diabetes patients were enrolled. Blood pressure, BMI, baPWV, HbA1c, Cholesterol, HDL, LDL & Triglycerides values were analysed. The ABI was measured with VP-

2000/1000-Colin Corporation, hyayashi komaki, Japan. PAD was considered when ABI measured was <0.9 in either leg.

Results: We studied 2778 patients (1681 men and 1097 women; mean age 50.4 ± 7.0 years; mean duration of diabetes 7.8 ± 5.9 years). The prevalence of PAD was 14.2% with men having a slightly higher prevalence (14.9%), as compared to women (13.2%). ABI was found to be significantly correlated with age ($r = 0.15$), duration of diabetes ($r = 0.09$), PWV ($r = 0.13$ for left and $r = 0.12$ for right) and DBP ($r = 0.13$). We did not find a significant correlation between measures of obesity (WHR) and PAD.

Conclusion: Using ABI, we found prevalence of PAD in 14.2% of type 2 diabetics which is comparable to western population. Risk factors significantly associated with PAD were - age, duration of diabetes, PWV and DBP. Considering ABI as a significant future CV risk marker, routine screening of diabetic population is advisable for future CV risk prevention.

TARGETING PHOSPHATIDYLINOSITOL-4, 5-BISPHOSPHATE METABOLISM IN ENDOTHELIAL INSULIN RESISTANCE AND DYSFUNCTION

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Insulin resistance refers to diminished biologic response of target cells to the hormone despite the presence of normal or elevated blood hormonal levels. Vascular insulin resistance has been linked with cardiovascular related morbidities and mortalities in diabetes mellitus and the metabolic syndrome. Existing data suggest reduced cellular levels of the phospholipid Phosphatidylinositol-4, 5-bisphosphate (PtdIns(4,5) P₂) and increased plasma membrane activity of Phospholipase C in insulin resistant L6 myotubes and Adipocytes. Here, an investigation of similar changes in endothelial cells (ECs) and their role in the pathogenesis of vascular insulin resistance is undertaken. Preliminary data obtained from EAhy.926 and Primary HUVECS pretreated with Angiotensin II and TNF alpha, both of which are associated with insulin resistance in vivo, have so far confirmed reduced insulin signalling via PI3Kinase-Akt-eNOS pathway. The levels of PtdIns(4,5) P₂ was also observed to be diminished in ECs induced with insulin resistance under similar cell culture conditions. Presently, the contribution of the several different PtdIns(4,5) P₂ metabolic pathways in bringing about the depletion of the cellular content of this signal lipid in endothelial cells are still

under investigation. The findings from this work would impact on the body of evidence supporting a role for PtdIns(4,5) P₂ metabolism in the pathogenesis of insulin resistance syndrome, possibly, leading to the identification of a likely therapeutic or prophylactic target for endothelial dysfunction, atherosclerosis and related health complications. Author's statement/willingness to present a poster if selected. I am expected by my institution to have my abstract accepted and to present a poster during this meeting and I am willing to do so. Failure to provide evidence that these conditions have been met would mean that I will not get the sponsorship from my bench.

ASSOCIATION OF INSERTION/DELETION POLYMORPHISM OF ANGIOTENSIN-I CONVERTING ENZYME GENE WITH CORONARY ARTERY DISEASE (CAD) IN ASIAN INDIANS

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Abstract: Angiotensin-1-converting enzyme (ACE) gene has established substantial attention in the recent years as a candidate gene for hypertension, cardiovascular diseases and type 2 diabetes. The aim of the present study was to investigate the association of ACE (I/D) polymorphism with coronary artery disease (CAD) in Asian Indians. A total of 662 subjects (330 CAD patients and 332 healthy controls) were examined for association of ACE gene (I/D) polymorphism and environmental risk factors. The mean age of the CAD patients and control subjects was 60.53 ± 8.6 years and 56.55 ± 7.7 years, respectively ($P = 0.000$). BMI values was significantly higher among CAD patients and control subjects (26.98 ± 4.9 vs 24.04 ± 4.7 , $P = 0.000$). We observed pronounced central obesity in both CAD patients and controls, even at the lowest BMI values (<23 kg/m²). Dyslipidemia was highly prevalent in CAD patients compared to control subjects. High frequency of DD genotype was observed in CAD patients have than that of control subjects (40% vs 28.3%). No significant difference was observed in the distribution of ID genotypes between CAD patients and control subjects. Logistic regression analysis of data demonstrate that DD genotype was associated with 1.8 fold increased risk of development of CAD in Asian Indians (OR = 1.8; 95% C.I. = 1.22-2.66; $P = 0.003$). The frequency of D allele was significantly higher in CAD patients ($P = 0.001$). No significant difference was observed in the clinical and biochemical characteristics of CAD patients and controls when the data was stratified according

to the genotypes of ACE gene. In conclusion, DD genotype of ACE gene may be associated with increased risk of CAD in north Indian population.

Key words: Coronary artery disease, ACE gene, North Indian, insertion/deletion polymorphism.

ASSOCIATION OF HYPERTRIGLYCERIDAEMIA WITH GESTATIONAL DIABETES AND ADVERSE PREGNANCY OUTCOMES

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Background: Plasma lipids and lipoproteins increase during pregnancy, but the mechanism is not completely understood, but appears to be partly caused by elevated oestrogen, progesterone and human placental lactogen. We aimed to determine whether high plasma triglyceride levels in the second trimester of pregnancy are associated with adverse pregnancy outcomes including, pre-eclampsia, preterm birth, gestational diabetes mellitus, and high uterine artery pulsatility index.

Methods: This was a prospective cohort study between 2008 and 2010. Plasma levels of low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglyceride were measured after 8 hours of overnight fasting. We compared the outcomes of 45 pregnant women who had high triglyceride levels (≥ 195 mg/dl) with 135 pregnant women with triglyceride levels < 195 mg/dl.

Results: The incidence of gestational diabetes (20% vs. 5.9%, $P = 0.03$), Preterm birth (24.4% vs. 5.9%, $P < 0.0001$), and Pre-eclampsia (17.8% vs. 3.7%, $P = 0.004$), in the high triglyceride group was significantly higher than that in the control group. The incidence of Increased pulsatility index in women with high triglyceride levels was higher than in women with low triglyceride levels but was not significant (17.8% vs. 3.7%, $P = 0.6$).

Conclusion: There is a positive relation between hypertriglyceridaemia and pre-eclampsia, preterm birth and gestational diabetes.

INSULIN RESISTANCE: ASSOCIATION WITH HEART AGING AND CELLULAR SENEESCENCE

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Introduction: Aging of the heart is associated with left ventricular (LV) hypertrophy and diastolic dysfunction. Insulin resistance (IR) is exacerbating aging-related changes in the heart. A strong associations exists between IR and heart failure, LV remodeling. One possible mechanism of IR-induced cardiac aging could be related to decreased telomeres length of leukocytes (LTL). LTL is a marker of replicative senescence. Our hypothesis is that IR led to attrition telomeres and senescent phenotypes in the heart.

Methods: We investigated 198 non-obese participants aged 60 to 85 years without CVD and diabetes. All volunteers underwent echocardiography, had an oral glucose tolerance test. HOMA-IR was calculated as fasting insulin (mU/ml) x fasting glucose (mmol/l) (mmol/l)/22.5. IR was diagnosed in case of HOMA-IR elevation > 2.5 based on reference. LTL was measured by real-time quantitative polymerase chain reaction.

Results: HOMA-IR was related to age ($\beta = -0.026$, $P = 0.015$) and LTL ($\beta = -0.176$, $P = 0.027$). HOMA-IR was correlated with LV wall thickness ($r = 0.489$, $P < 0.001$), E/Em ($r = 0.379$, $P < 0.01$), E/A ($r = -0.320$, $P < 0.01$), Em/Am ($r = -0.342$, $P < 0.01$). LTL was significantly associated to diastolic function indices regardless of age ($P < 0.001$). Older subjects with higher HOMA-IR had a shorter telomeres ($P = 0.046$) and more expressed LV hypertrophy and diastolic dysfunction to compared to subjects with normal HOMA-IR. The groups were comparable in the proportion of smokers, levels of blood pressure and BMI.

Conclusions: Our findings suggest that IR is associated with signs of the heart aging and shorter LTL. Accelerated telomere attrition appears to be the mechanism by which impaired IR develops into cardiac aging.

IMPACT OF METABOLIC SYNDROME ON IN-HOSPITAL OUTCOMES IN ACUTE ST ELEVATION MYOCARDIAL INFARCTION- INDIAN EXPERIENCE

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Introduction: Aim of the study was to observe the impact of metabolic syndrome (MS) on in-hospital outcomes in patients of Acute ST Elevation myocardial infarction (Acute-STEMI) and to assess the relative influence of MS components on these adverse outcomes.

Methods: In a cross-sectional observational study, 100 consecutive patients of Acute-STEMI, who underwent PCI at our center between 1st November 2013 and 31st March 2015, were enrolled. MS was defined by NCEP-ATPIII criteria. Patients were observed for adverse outcomes during hospital stay. Primary outcomes were mortality and heart failure- measured by killip class. Multiple regression analysis was done to find the association between MS and outcomes.

Results: The prevalence of MS in Acute-STEMI patients was 34%. Prevalences for MS components were found to be low-HDL (94%), hyperglycemia (85%), hypertension (68%), abdominal obesity (65%) and high-triglyceride (50%). Incidences of heart failure (killip >I), cardiogenic shock, reduced ejection fraction and renal failure (eGFR \leq 60 ml/min) were higher in the MS group. Total mortality was 4, all in MS-group. On multivariate analysis, MS was found to be an independent predictor of heart failure ($P < 0.001$, $r^2 = 0.59$), cardiogenic shock ($P = 0.024$) and renal failure ($P = 0.006$) even after adjusting for confounding variables. However, MS was not associated with mortality ($P = 0.997$). Out of the MS components, hyperglycemia was strongly associated with heart failure ($P = 0.001$) while hypertension with renal failure ($P = 0.021$).

Conclusion: MS is an independent predictor for the development of heart failure, cardiogenic shock and renal failure, but not for hospital mortality, in Acute-STEMI patients.

ANTIHYPERGLYCAEMIC POTENTIAL OF PSIDIUM GUAJAVA LEAF IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Introduction: *Psidium guajava* (PG) leaf is known to have a blood-glucose lowering effect in diabetic rats. The aim of the present study was to carry out a phytochemical study of PG leaf extract; investigate its protective effect on pancreas, its effect on muscle protein kinase B (PKB/Akt) and also on liver and adipose tissue hormone sensitive lipase (HSL) activity in streptozotocin induced diabetic male Sprague-Dawley rats.

Methods: Diabetes was induced in male Sprague-Dawley rats with a single dose of 40 mg/kg body weight streptozotocin. The aqueous extract of *Psidium guajava* leaves was used to treat both normal and diabetic animals (400 mg/kg body weight) for 2 weeks while control animals were treated with the vehicle.

Results: After 2 weeks of treatment, PG lowered blood glucose and protected pancreatic tissue from diabetic damage. The treatment activated protein kinase B (PKB/Akt) and decreased hormone sensitive lipase activity in liver and adipose tissue. PG also increased the amount of glycogen in the liver. GC-MS analysis of the aqueous extract of PG indicated the presence of phenolic compound and triterpenoids.

Conclusions: We conclude that PG has antidiabetic and hypolipidaemic effects, and these effects may be associated with the presence of phenolic compound and triterpenoids. PG also decreased hormone sensitive lipase activity and activated protein kinase B (PKB) in the insulin signalling pathway.

NEUROPROTECTIVE EFFECT OF QUERCETIN IN DIABETIC RAT RETINA

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Introduction: Diabetic retinopathy (DR) is a severe complication of diabetes and is the leading cause of blindness among working adults worldwide. DR is being widely rec-

ognized as a neurodegenerative disease of the retina, since, retinal neurons are vulnerable to be damaged early in the disease progression. Neurotrophic factors play an important role in the functional maintenance of neuronal cells and dysregulation has been found to cause neurodegeneration in diabetic retinopathy.

Objective: In this study, we employed polyphenolic compound, quercetin to treat streptozotocin-induced diabetic rats and analyzed the inhibitory factors of neurodegeneration in the retina.

Methods: We measured the level of BDNF, NGF, TrkB, synaptophysin and caspase-3 activity in the diabetic retina with and without quercetin treatments and compared with non-diabetic rats. We employed ELISA to determine the level of BDNF and immunoblotting techniques to determine the expression of those factors. Caspase-3 analyzed by biochemical method.

Results: Our analyses indicate that quercetin treatment to diabetic rats caused a significant increase in the level of those neurotrophic factors and inhibited the caspase-3 activity in the diabetic retina.

Conclusion: Thus, quercetin, may protect the neuronal damage by ameliorating the level of neurotrophic factors and also by inhibiting of apoptosis in the retina of diabetic rats. However, further studies needed to understand the effect of this drug on the beneficial effects in inhibiting oxidative stress and inflammation in diabetic retinas.

RANDOMIZED CONTROLLED TRIAL OF LIFESTYLE INTERVENTION FOR TYPE 2 DIABETES PATIENTS IN KUWAIT AND ITS IMPACT ON GLYCAEMIC CONTROL AND THE QUALITY OF LIFE PRELIMINARY RESULTS

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Introduction: The prevalence of diabetes is increasing in the Gulf States and it is therefore important to investigate potential methods to improve outcome by lifestyle modification in primary care.

Aims: The primary aim of the *Randomized Controlled Trial of Lifestyle Intervention for Type 2 Diabetes Patients in Kuwait* is to evaluate the effectiveness of a group based

structured lifestyle intervention, including nutrition and physical activity in attaining optimal glycaemic control. The secondary aim is to investigate how cultural and other factors affect compliance to lifestyle interventions and outcomes.

Methods: The study is conducted as a 9-month 2-arm randomised trial in Kuwaiti men. The intervention group (n = 40) receives regular educational interventions with specific focus on different aspects of lifestyle modifications, such as exercise and dietary changes. The control group (n = 20) will receive a standard treatment. The participants were recruited at the Al-rehab polyclinic in Kuwait. Eligible diabetes patients, between 30-65 years old, who have been diagnosed with Type 2 Diabetes, were selected. The study was approved by the [ethical permission from Reading University in the UK, and Kuwait Institute of Medical Specialization, (KIMS), Medical Research Ethics Committee in Kuwait] and all participants provided informed consent. The lifestyle intervention was conducted after the baseline visit. The intervention group attend a group discussion session every two weeks. A text was sent before the session as a reminder, also regular texts messages, including dietary and physical activity advices were sent to the intervention group. The duration of the lifestyle change group sessions is sixty minute meeting with the 20 participants was run, a total of four accomplished sessions during the RCT. Each session had a title, explained by its aims and the description of each session.

Results: 20 participants were randomised to intervention, while 20 participants were randomised to usual care. Descriptive statistics were measured for the baseline parameters, using a *t*-test for normally distributed and Mann-Whitney-U test for non-parametric data. As the study is still running, the intervention group will be strictly be followed after the end of the educational session by sending frequent text messages, including dietary and physical activity advices.

Discussion: In this study, we investigate whether new methods of lifestyle interventions, which can be easily implemented in general practice, can improve glycaemic control in diabetes patients in Kuwait. The HbA1c is the primary endpoint. For the baseline, the mean HbA1c was $8.78\% \pm 1.87$ in the intervention group compared to $8.49\% \pm 1.42$. There was no significant difference in the other parameters between both groups.

CAPSAICINOIDS FROM CAPSICUM EXTRACT INHIBITS PANCREATIC LIPASE, ENHANCED LIPOLYSIS AND OTHER BIOLOGICAL ACTIVITIES

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Background: Digestion and absorption of dietary lipids by pancreatic lipase, a major source of excess calorie intake, can be targeted for development of anti-obesity agents. Capsaicinoids may have the potential therapeutic value for weight loss, cardio-protective influence, anti-lithogenic effect, anti-inflammatory, analgesia, thermogenic, and digestive stimulant action and modulation of intestinal ultra-structure so as to enhance permeability to micronutrients in the gastrointestinal (GI) system. It has been shown that capsaicinoids are potential agonists of capsaicin receptor (TRPV1).

Objectives: To study the effects of capsaicinoids from capsaicin extract (CPX) on pancreatic lipase, lipolysis and other biological activities.

Methods: Pancreatic lipase activity was measured using 4-methylumbelliferyl oleate (MU Oleate) as a substrate via a fluorescence kinetic assay. 3T3L1 cells were treated with CPX (100µg/ml) at different time points. Lipolysis was assessed using glycerol release as a biomarker. In another study, 3T3 L1 pre-adipocytes were treated overnight with CPX. RNA was isolated and cDNA prepared. Real time PCR was performed on a selected list of genes using standard protocols.

Results: CPX displayed a strong potent inhibitory effect of pancreatic lipase (PL) and compared to Orlistat. IC₅₀ for CPX was 5.4 (µg/ml) compared to Orlistat (0.53 µg/ml). CPX enhanced the lipolysis after 24h treatment. The ratio of released glycerol/protein content was 1.59, compared to positive control: isoproterenol (ratio: 1.60). CPX reduced fat accumulation by down-regulating SCD-1 and C/EBPα in 3T3Li adipocytes.

Conclusion: These observations suggest that CPX has inhibitory effects on PL, decreases fat accumulation by adipocyte differentiation inhibition and stimulates lipolysis on adipocytes. Therefore, CPX could be further studied and developed as a functional food in helping the treatment of postprandial lipidemia and/or prevention of weight gain and weight management.

ANEMIA IN PATIENTS WITH EARLY DIABETIC NEPHROPATHY: PATHOGENESIS AND CLINICAL IMPLICATIONS

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Anemia is a common complication of diabetic nephropathy (DN) with a negative prognostic value. In this study we assessed the contribution of different pathogenic factors for anemia development and clinical correlates of hemoglobin (Hb) level in early DN.

We investigated 95 anemic patients with type 2 diabetes mellitus and CKD stages 1-3. GFR was estimated by Cockcroft-Gault formula. In addition to routine tests we measured serum levels of erythropoietin (EPO), ferritin, vitamin B12, folate, interleukin-1β (IL-1β), interleukin-6 (IL-6) and tumor necrosis factorα (TNFα) using immunoassay.

We found EPO deficiency in 46,3%, low ferritin – in 11,6%, vitamin B12 deficiency – in 1,1% and folate deficiency – in 2,1% patients. 61% had normochromic anemia, 27% – hypochromic anemia, 12% – hyperchromic anemia. The prevalence of EPO deficiency was progressing with the decline in GFR. Hb level had no significant correlations with age and glycemic control. Elevated serum cytokine levels were observed in the following percentage of patients: IL-1β – 86,3%, IL-6 – 70,5%, TNFα – 21,1%. Hb level correlated negatively with their concentrations. Spearman's correlation coefficients were as follows: rs = -0,273 (Hb/IL-1β), rs = -0,500 (Hb/IL-6), rs = -0,311 (Hb/TNFα), P<0,05. The results of the study suggest that anemia in patients with early DN is often related to EPO deficiency and systemic inflammation. Given this evidence for complex pathogenesis of anemia in DN, comprehensive investigation is essential for effective treatment. The study was supported by the President Grant for Government Support of Young Russian Scientists MK-5632.2015.7.

ADIPOCYTE FATTY ACID BINDING PROTEIN MEDIATES ADAPTIVE THERMOGENESIS VIA INDUCING INTRACELLULAR THYROID HORMONE CONVERSION

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Introduction: Adaptive thermogenesis is a defense mechanism that organism dissipates energy in the form of heat

protecting against hypothermia or obesity. Adipocyte fatty acid binding protein (A-FABP) is an adipokine that regulates fatty acid trafficking and signaling. A-FABP deficiency alleviates metabolic dysfunction while exacerbates high fat diet-induced obesity in mice. Here, we explored the role and potential mechanism whereby A-FABP modulates adaptive thermogenesis.

Methods: (1) A-FABP knockout (KO) mice and their wide-type (WT) littermates were fed with standard chow or high fat high cholesterol (HFHC) diet for 24 weeks. (2) WT or KO mice with or without recombinant A-FABP (rA-FABP) replenishment were treated with thyroxine (T4) or 3,3,5-triiodothyronine (T3). Thermoregulatory ability of mice was accessed by measurement of energy expenditure and cold tolerance test. T4 and T3 concentrations was measured, brown adipose tissue (BAT) recruitment was assessed by biochemical analysis.

Results: A-FABP deficiency impeded HFHC diet- and cold-induced energy expenditure and attenuated T4 to T3 conversion in mice. Restoration of rA-FABP significantly improved thermogenesis by promoting BAT recruitment and browning of subcutaneous white adipose tissue (sWAT) in A-FABP KO mice. The induction of type II deiodinase (D2), key enzyme responsible for T4 to T3 activation, was abolished in BAT of KO mice while rA-FABP replenishment reversed T4-induced energy expenditure.

Conclusion: A-FABP promotes adaptive thermogenesis by enhancing intracellular T4 to T3 conversion in BAT through its regulation on D2 expression, further induces the expression and activation of UCP-1 for thermogenesis. Acknowledgement: This work was supported by general research fund (HKU 766812M) and Shenzhen Basic Research Grant (JCYJ20140903112959965).

PREVENTIVE EFFECTS OF COMBINATION OF *TERMINALIA ARJUNA* AND *EUGENIA JAMBOLANA* IN ISOPROTERENOL INDUCED MYOCARDIAL INFARCTION IN RATS – A MECHANISTIC APPROACH

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Abstract: This study was aimed to evaluate the combined preventive effects of hydroalcoholic extract of *T. arjuna* (HETA) and hydroalcoholic extract of *E. jambolana* (HEEJ) by assessing the oxidative stress, cardiac markers, markers of inflammation and histopathological studies

in ISP-induced myocardial infarction in rats. Male Wistar rats were pre-treated with a combination of HETA and HEEJ (100, 200 and 400 mg/kg) daily for 30 days. During the pre-treatment period, ISP (85 mg/kg) was injected to rats on 28th and 29th days at an interval of 24 hr for two days. The levels of cardiac markers, markers of inflammation and oxidative stress parameters were assayed and further confirmed by histopathological studies. ISP treated rats showed significant increase in the levels of MDA, SGOT, CK-MB, cTnI, CRP, IL-6 and TNF- α . Combined pre-treatment with HETA and HEEJ restored all the parameters studied, dually justified in histopathological findings. The possible mechanism for the preventive effects of combined pre-treatment of HETA & HEEJ could be attributed to scavenging free radical, decreasing MDA, cardiac markers, markers of inflammation and strong antioxidant property (GSH,SOD). Thus this study demonstrated the combined pre-treatment may have better option of choice for attenuation of ill effects of ISP-induced myocardial infarction and may have significant impact on patients suffering from IHD.

Key words: *Terminalia arjuna Eugenia jambolana, isoproterenol, myocardial infarction, oxidative stress, apoptosis.*

SYSTEMS BIOLOGY OF OBSTRUCTIVE SLEEP APNEA AND METABOLIC SYNDROME

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Objective: Despite the prolific data that suggests positive association between obstructive sleep apnea (OSA) and metabolic syndrome (MS), the functional relationship between OSA and MS remains unclear. Therefore, we aimed to traverse the genetic-association between OSA and MS using systems biology approach.

Methods: Candidate genes for OSA and MS were extracted from Comparative Toxicogenomics Database (<http://ctdbase.org/help/goDisease>). Overlapping genes associated with OSA and MS were then assembled by Functional Enrichment analysis tool (FunRich). Biological functions of the overlapping genes were then identified by using the Gene Ontology (GO) approach using Protein Analysis Through Evolutionary Relationships (PANTHER) tool. GO is a bioinformatics resource tool that uses structured controlled vocabularies (ontologies) to describe the *molecular functions* or activities of a gene product, *biological processes* in which a gene product is involved and the *cellular components* in which a gene product is located.

Results: In total, 15,228 and 6586 genes associated with MS and OSA respectively. Among these, 5322 genes overlapped between OSA and MS. GO analyses revealed that genes associated with metabolic diseases, inflammation/oxidative stress, neurotransmitter regulation, behavior/cognitive function and neurological diseases (Alzheimer's/Parkinson's disease) were 25.2%, 13.6%, 12.8%, 8.9% and 4.8% respectively. Other biological functions (i.e., cellular processes, homeostasis and reproduction etc.,) contribute to 34.7% of the biological functions.

Conclusions: Large proportion of biological functions were shared between OSA and MS. This support the concept that screening of OSA among individuals with MS. Future lifestyle intervention programs for chronic care management should also focus sleep as an interventional component to attain maximum benefits.

STUDY OF INDUCIBLE NITRIC OXIDE SYNTHASE MUTANT AND ENDOTHELIAL DYSFUNCTION ALONG WITH PRO-INFLAMMATORY MARKERS IN CORONARY ARTERY DISEASE

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Objective: The prevalence of coronary artery disease (CAD) in North Indian population varies from 7 to 10%. Patho-physiological processes in coronary artery disease are influenced by genetic factors. Vascular function and endothelial derived factors are affected by pro-inflammatory cytokines which leads to the activation of Inducible nitric oxide synthase (iNOS) during inflammation. The aim of this study was to look for a relationship between the C150T polymorphisms of the iNOS and endothelin dysfunction in Coronary Artery Disease (CAD) and correlation with pro-inflammatory markers.

Methodology: 150 Angiographically confirmed coronary artery disease patients attending the cardiac clinic of G B Pant hospital, New Delhi and 90 healthy people with no known risk factors for CAD were enrolled in this case-control study. Blood samples were collected and analyzed for nitric oxide (Methew et al), endothelin-1, inflammatory markers (by Elisa), iNOS (C150T) gene polymorphism (by PCR RFLP).

Results: Patients with CAD had increased levels of, IL-2, IL-6, and TNF- α , endothelin-1 and decreased level of nitric oxide as compared with healthy people ($P < 0.0001$). Significant positive correlation was seen between endo-

thelin-1 and cytokines levels and negative correlation was found between NO and cytokines levels CAD patient ($P < 0.001$). C150T iNOS genotype distributions in patients with CAD (C 150 T: CC: 87.3%, CT: 12.6%, TT: 0%) was found to be significantly different from those in patients without CAD (C 150 T: CC: 96.6 %, CT: 3.3 %, TT: 0%). Significant differences were found in genotype/allele (C150T) distribution between two groups.

Conclusion: Raised levels of pro-inflammatory markers may have a role in the development of coronary heart disease. A larger group studies are required to establish the link of these markers with the disease. Endothelial dysfunction is characteristic features of coronary artery disease and the iNOS C150T polymorphism may contribute by affecting NO levels.

THE IMMUNOLOGICAL IDENTIFICATION OF PAI-1 (PLASMINOGEN ACTIVATOR INHIBITOR-1) ON HUMAN BREAST CANCER TISSUE AND NORMAL MAMMARY GLAND

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Introduction: In primary breast cancer, urokinase-type plasminogen (uPA) and its inhibitor plasminogen activator inhibitor type 1 (PAI-1) are the first novel tumor biological markers (1-3, 10). High expression of PAI-1 is associated with marked tumor spreading and poor prognosis. In primary breast cancer, uPA and PAI-1 are the first novel tumor biological markers for which level-I evidence for their prognostic impact according to the recently proposed criteria of Hayes et al. has provided (4, 5, 7). Patients with high tumor antigen levels of either factor have significantly worse survival than patients with low levels (6, 8, 9). Only a few studies have investigated the relation between PAI-1 levels and breast cancer. In this study, we aimed to compare levels of PAI-1 in tissue suspensions in samples from breast cancer and normal tissues.

Material And Methods: We included 30 consecutive patients with operable breast cancer and another 30 individuals whose biopsies were benign. All the patients were informed on the study and consented for reserving a part of the biopsy specimen for research purposes. A small part of those biopsies sent to frozen section were collected and immediately stored at -80°C until assayed. After all the

specimens were collected, they were weighed by high sensitive pair of scales. They were then homogenized in homogenization solution. PAI-1 were studied in homogenized solutions by ELISA .ZYMUTEST PAI-1 Activity RK019A (Complete ELISA kit for Tissue-Plasminogen Activator Inhibitor Type I Activity) Statistical analyses were performed by using Statistical Package for Sciences.

Results: There is no significant difference between the two groups according to age and body mass index ($P>0.05$). In both groups of menopausal women PAI-1 levels were lower according to nonmenopausal women ($P = 0.02$). In the group with breast tumor, the median PAI-1 level was found to be 0.18+0.007 and in control group 0.39+0.09. The difference was found to be statistically significant ($P = 0.001$). In both groups there was no significant difference related with other variables.

Conclusion: PAI-1 and uPA are the only novel tumor biological factors that have reached level-I evidence with regard to their prognostic impact in primary breast cancer (1,10) . Urokinase-type plasminogen activator (uPA) and its inhibitor (PAI-1) play essential roles in tumor invasion and metastasis. High levels of both uPA and PAI-1 are associated with poor prognosis in breast cancer patients (2). In our study PAI-1 levels in breast cancer tissue is lower than normal mammary tissue. This result shows that the low level of PAI-1 levels in mammary tissue is a high risk of breast cancer development.

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THE IMMUNOLOGICAL IDENTIFICATION OF LEPTIN ON HUMAN BREAST CANCER TISSUE AND NORMAL MAMMARY GLAND

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Introduction: Incidence of cancer is higher in obese individuals which has not been clearly understood. The relationship of obesity as a risk factor for cancer is complex. Leptin levels is high in individuals with breast cancer (1-3). In this study we aimed to compare levels of leptin in tissue suspensions in samples from breast cancer and normal tissues.

Materyal And Methods: We included 30 consecutive patients with operable breast cancer and another 30 individuals whose biopsies were benign. All the patients were informed on the study and consented for reserving a part of the biopsy specimen for research purposes. They were then homogenized in homogenization solution. Leptin were studied in homogenized solutions by ELISA using Human Leptin elisa kit . Body mass indexes for all the individuals were calculated. Menopausal status, types of surgery, tumor size, lymph node status, hormonal status for patients. Statistical analyses were performed by using Statistical Package for Sciences.

Results: Normal mammary epithelial cells did not express a significant level of leptin, whereas carcinoma cells showed positive staining for leptin 25 (83%) cases (4, 5). Both normal epithelial cells and carcinoma cells expressed a significant level of leptin (6-9). However, overexpression of leptin, as determined by staining intensity. The expression of leptin showed a significant correlation with the level of leptin expression.

Conclusion: Leptin may have a promoting effect on the carcinogenesis and metastasis of breast cancer, possibly in an autocrine manner. Functional inhibition of leptin may be effective for the prevention and treatment of breast cancer.

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THE IMPACT OF PIOGLITAZONE THERAPY ON GLYCEMIC CONTROL, BLOOD PRESSURE AND INFLAMMATORY MARKERS IN PATIENTS WITH DIABETES MELLITUS

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Aim: The aim of our study was to investigate the effect of pioglitazone on glycemic and blood pressure control, on inflammation markers in diabetic patients.

Patients and Methods: Forty-nine out patients diabetic patients who had been followed up for 2.7 years and HbA1c was >7% were included in the study. The patients had never received thiazolidinedione therapy before. Clinical, metabolic variables, high-sensitive C-reactive protein (hsCRP), homocysteine (HCY) and asymmetric dimethylarginine (ADMA) levels were measured. 30 mg pioglitazone were administered. The patients were followed up for six months and all the measurements were re-evaluated for comparison.

Results: Body mass index (BMI) significantly increased after treatment. Fasting glucose, HbA1c and HsCRP were

decreased. Insulin resistance was improved and HOMA-IR index was decreased after pioglitazone treatment [8 (± 6.5) vs 4 (± 3.1); $P < 0.0001$]. Pioglitazone improved lipid metabolism. Mean total cholesterol and LDL cholesterol levels were decreased and HDL cholesterol was increased after treatment. The decrease in triglyceride and homocysteine levels did not reach significance. Mean ADMA level did not change after therapy [0.62 (± 0.39) vs 0.61 (± 0.44); $P = 0.85$].

Conclusion: Pioglitazone treatment in type 2 DM produced significant improvements in measures of glycemic control, plasma lipids, blood pressure and homocysteine levels. Pioglitazone had no influence on ADMA levels.

Keywords: Asymmetric dimethylarginine (ADMA), diabetes mellitus, high-sensitive C-reactive protein, homocysteine, insulin resistance, pioglitazone

CAROTID INTIMA MEDIA THICKNESS IN LATINO ADOLESCENTS WITH DEBUT OF TYPE 2 DIABETES MELLITUS

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Introduction: It has been described the strong relationship between the carotid intima-media thickness (CIMT) and insulin resistance in adults diagnosed with T2D. However, there are no studies that assess the CIMT Latin American adolescents with debut of T2D. We aimed to evaluate the expected CIMT values in this population and to assess its relationship with some insulin-resistance-laboratory parameters, in order to identify asymptomatic endothelial dysfunction and to prevent vascular complications in this target group.

Methods: This is a cross-sectional study of 81 Latin American patients who debut T2D in adolescents aged between 12 to 30 years, distributed in three groups: (i) 27 with debut of T2D, (ii) 26 were overweight/obese non-diabetic; and (iii) 27 were lean non-diabetic, from Arzobispo Loayza National Hospital in Lima, Peru. Laboratory evaluation (fasting glucose, HbA1C, lipid profile and us-CRP) and Doppler Ultrasound were performed to evaluate their relationship with the CIMT of the common carotid in these three groups.

Results: There was a significant difference of CITM means between the three groups of conditions (one-way ANOVA,

$P = 0.016$). Older age, higher levels of LDL and being overweight/obese were independently associated with a higher CIMT mean in the multivariate model. Type 2 diabetes was strongly associated with CIMT, although not statistically significant (adjusted β : 23.90 [95% CI: -5.03 to 52.82]).

Conclusions: Adolescents with T2D had greater CIMT than lean-non diabetic. In the multivariate model just overweight/obese was associated with a greater CIMT-mean. The only laboratory parameter that showed association with CIMT was serum level of LDL.

IMPACT OF OBESITY ON DIABETES CONTROL AND IT'S COMPLICATIONS

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Background: Obesity and diabetes are common public health problems among Saudis. Among diabetics, weight management is more challenging, because of the weight-promoting effect of most glucose-lowering therapies.

Aim of Study: To explore the impact of obesity and overweight on diabetes mellitus control and diabetes-related complications among type 2 diabetics.

Patients and Methods: A total of 111 (39 males and 72 females) type 2 Saudi diabetics attending Family Medicine and Diabetes Centers, were included in this study. Demographic characteristics, body weight, height, waist and hip circumference Fasting plasma glucose and HbA_{1c} were measured.

Results: Mean age of participants (SD) was 55.4 (12.6) years. According to body mass index (BMI), 11 patients (9.9%) had BMI less than 25 kg/m², 32 (28.8%) were overweight (BMI >25 kg/m² and <30 kg/m²), while 68 (61.3%) were obese (>30 kg/m²). According to the waist-to-hip ratio, 89 patients (80.2%) were obese. Mean fasting plasma glucose (FPG) was significantly different according to BMI (103.7 + 11.3 mg/dL for normal BMI, 164.5 + 55.0 mg/dL for overweight patients and 196.5 + 75.4 mg/dL for obese patients, respectively, $P < 0.001$). Similarly, HbA_{1c} differed significantly according to BMI (6.5 + 0.5 for normal BMI, 8.4 + 1.1 for overweight patients and 9.1 + 1.6 for obese patients, respectively, $P < 0.001$). Moreover, mean FPG was significantly different according to waist-hip ratio (145.1 + 82.0 mg/dL for normal ratio and 186.3 + 66.9 mg/dL for high ratio patients, $P = 0.015$). Similarly, HbA_{1c}

differed significantly according to waist-hip ratio (7.3 + 1.5 for normal ratio patients and 9.0 + 1.4 for high ratio patients, $P < 0.001$). Two thirds of patients were hypertensive (66.7%), 21.6% had retinopathy, 17.1% had nephropathy, 14.4% had neuropathy, 17.1% had diabetic foot, while 19.8% had coronary artery disease. Prevalence rates for all complications among type 2 diabetics were higher among obese than non-obese patients, with significant differences regarding hypertension ($P = 0.004$), retinopathy ($P = 0.030$) diabetic foot ($P = 0.017$); nephropathy ($P = 0.015$) and coronary artery disease ($P = 0.045$). **Conclusions:** Prevalence of overweight/Obesity is high among type 2 Saudi diabetics. Diabetes control is highly impaired among overweight/obese diabetics. Diabetes related complications are more common among obese diabetics. Weight reduction is an important step toward achievement of diabetes control and prevention of diabetes-related microvascular and macrovascular complications.

Keywords: Diabetes, type 2, Saudi, Overweight, Obesity, body mass index, waist-hip ratio, diabetes control, fasting plasma glucose, HbA_{1c}, microvascular complications, macrovascular complications.

ANTIDIBETIC EFFECT OF APIUM GRAVEOLEN IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Aim and Objective: To investigate antidibetic effect of Apium graveolen L. (Celery seeds) on blood glucose and insulin concentrations in streptozotocin (STZ) induced diabetic rats

Methods: Forty Sprague Dawely rats weighing from 180 to 230 grams were randomly divided into four experimental groups A, B, C & D, each containing ten (10) rats. Diabetes was induced by intraperitoneal administration of STZ (60 mg/kg) in groups B, C & D, while group A served as normal control. The experimental animals became diabetic within 48 to 72 hours after administration of STZ., Group B rats were taken as diabetic control. Alcoholic extract of Apium Graveolen, the test drug was administered (400 mg/kg) orally to experimental group C, while group D received standard drug glibenclamide.induced diabetic rats for six weeks. Normal control group A and diabetic control B received only normal saline solution orally. Blood samples were collected from experimental groups after 43 days, 24 hours of the last dose. ANOVA and Tukey HSD (Honestly Significant Difference) test applied to all groups.

Results: The results show Apium Graveolen extract treatment caused a statistically significant decrease in the elevated serum glucose levels and increase in the serum insulin concentrations in test group C as compared to group B.

Conclusion: Findings of present study provide evidence for traditional use of Apium Graveolen in the control of diabetes.

Key Word: *Streptozotocin, Apium graveolen*

CANAGLIFLOZIN IMPROVES RISK FACTORS ASSOCIATED WITH METABOLIC SYNDROME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND METABOLIC SYNDROME

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Background: Metabolic syndrome (MetS) combines several factors associated with increased risk of cardiovascular diseases and Type 2 Diabetes Mellitus (T2DM). Canagliflozin (CANA), a sodium-glucose co-transport 2 inhibitor, improves glycemic control by reducing renal glucose reabsorption, increasing urinary glucose excretion. This analysis assessed the effect of CANA on MetS in patients with T2DM and MetS.

Methods: Pooled data from 4 randomized trials of patients with T2DM receiving once-daily CANA 100mg, 300mg, or placebo (PBO) for 26 weeks were analyzed. MetS was defined as patients having ≥ 2 of the following criteria additionally to T2DM diagnosis: triglycerides (TG) ≥ 150 mg/dL; high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL (men), < 50 mg/dL (women); waist circumference (WC) ≥ 102 cm (non-Asian men), ≥ 88 cm (non-Asian women), > 90 cm (Asian men), > 80 cm (Asian women); diagnosis of hypertension or systolic blood pressure (SBP) ≥ 130 mmHg or diastolic BP (DPB) ≥ 85 mmHg. Changes in A1C, fasting plasma glucose [FPG], BP, WC, body weight [BW], body mass index [BMI] and lipids were evaluated after 26 weeks.

Results: 1,840/2,313 (80%) of patients with T2DM met the MetS criteria. The proportions of patients meeting 3, 4, or 5 MetS criteria were 37.8%, 33.8%, and 17.3%. After 26 weeks, CANA treatment reduced A1C, FPG, SBP, DPB, WC, BW, and BMI in a dose-dependent manner (Table). In addition, LDL-C increased by 4.6 mg/dL (CANA 100mg) or 8.5 mg/dL (CANA 300 mg) vs. PBO, with increases in

HDL-C and reductions in TG (300 mg only) with CANA. CANA was generally well tolerated.

Conclusion: Treatment with CANA 100mg or 300mg improved all components of MetS in patients with T2DM.

IMEGLIMIN, A NEW ORAL ANTI-HYPERGLYCEMIC AGENT CONTROLS BOTH FASTING AND POST-PRANDIAL GLUCOSE THROUGH AN IMPROVEMENT IN BOTH INSULIN SECRETION AND INSULIN SENSITIVITY

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Key words: *Imeglimin, glycemic control, insulin secretion, insulin sensitivit*

Imeglimin is a novel glucose-lowering agent that targets mitochondrial bioenergetics and improves insulin secretion and sensitivity. This trial assessed the effect of Imeglimin on fasting (FPG) and post-prandial glucose (PPG) control in patients with type 2 diabetes, previously treated with metformin monotherapy. During this multi-center, double-blind, placebo-controlled, parallel-group, 18-week phase II study and after a 4-week wash-out period, fifty-nine patients (52.5% female; mean age, 56.4 years; A1C, 8.13%; BMI, 32.9 kg/m²) were randomized to either Imeglimin 1,500 mg BID or placebo. The primary efficacy endpoint was placebo-adjusted reduction of AUC glucose from baseline during a 3-hour OGTT; secondary endpoints included changes in FPG, A1C, insulin, C-peptide, AUC insulin or C-peptide/glucose ratio, insulin secretion (insulinogenic index) and insulin sensitivity (Stumvoll) derived indexes.

Imeglimin, versus placebo, significantly reduced AUC glucose from baseline (-439.2 mmol/L; -17% , $P = 0.001$), the 2-hour post-dose FPG (-1.22 mmol/L; -16% , $P = 0.022$) and the A1c by 0.62% ($P = 0.013$). Imeglimin increases both insulin secretion -as evidenced by an increase in 1/ the incremental AUC insulin or C-peptide over glucose ratio ($P = 0.025$ and 0.004 , respectively) and 2/ the insulinogenic index ($P = 0.025$)- and insulin sensitivity as indicated by an increase in the Stumvoll index ($P = 0.001$). One patient (3.3%) on Imeglimin required glycemic rescue treatment compared to 10 patients (34.5%) on placebo. Body weight remained stable. Imeglimin was well tolerated with no reported serious treatment-related adverse events. In conclusion, Imeglimin has a unique profile, enabling control of FPG and PPG by improving both insulin secretion and insulin sensitivity, with a good safety profile.

EFFECTS OF BARIATRIC SURGERY ON ADIPONECTIN, BILE ACIDS, FIBROBLAST GROWTH FACTOR-19, AND INCRETIN HORMONES IN OBESE ASIAN PATIENTS WITH TYPE 2 DIABETES

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Obesity is a serious healthcare problem worldwide. Ten percent of adult Singaporeans are obese and the obesity rate is increasing at approximately 1% per year. Bariatric surgery, such as Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) offers a very effective and sustainable solution for weight loss and glycemic control; however, the underlying pathophysiological consequences and metabolic cascades attributed to these procedures remain unclear. To this end, bariatric procedures were performed in 24 obese type-2 diabetic patients (BMI = 40.8 ± 5.5 kg/m²). Fasting adiponectin, bile acids (BA), and fibroblast growth factor-19 (FGF-19) were measured; oral glucose tolerance test (OGTT) samples were collected (baseline, 30-, 60-, 90-, 120-min, post-prandial) to deter-

mine incretin hormones concentrations (pre-surgery and 1-mo. post-surgery).

Our initial results indicate, at 1-mo. post-surgery, BMI was decreased significantly (36.2 ± 6.7 kg/m², $P < 0.05$, vs pre-surgery), while percentage change of fasting adiponectin and FGF-19 increased significantly by $159.8 \pm 79.3\%$ and $212.3 \pm 83.9\%$, respectively (vs pre-surgery). No significant change in fasting BA concentration was observed. Further, OGTT data reveal levels of incretin hormones (PYY, active GLP-1, and oxytomodulin) elevated significantly ($P < 0.05$, vs pre-surgery) and peaked at 30-min post-prandial. Eighty percent of the diabetic patients show a marked improvement in insulin sensitivity (HOMA-IR, decreased from 10.7 ± 7.0 to 5.4 ± 3.9 mmol/L.mU/L). These observations were ascribed to a shift in the preferential energy metabolism triggered by the bariatric surgery and changes in adipocytokines could lead to the rapid resolution in insulin resistance. Our findings can shed light into metabolic impacts of bariatric surgery and might elucidate novel drug targets for treating diabetes.

EFFECT OF CARDIAC REHABILITATION ON GLUCOSE EXCURSION IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Purpose: We aimed to investigate the effect of cardiac rehabilitation (CR) on glucose excursion.

Methods: Seventy-seven acute coronary syndrome (ACS) patients who underwent percutaneous coronary intervention and 75g oral glucose tolerance test (OGTT) from 2011 to 2014 were enrolled. OGTT was performed twice apart 6-9 months to assess glucose metabolism and dynamic state of insulin secretion. Change of glycemic profile was compared between patients who participated in CR and those who did not. Glucose excursion was defined as follows: maximum glucose level – minimum glucose level during OGTT.

Results: Thirty-four patients participated in CR program and 43 patients did not. During the first OGTT, no significant difference was observed in the baseline glucose profile and serum insulin level between two groups. During the second OGTT, patients with CR had significantly higher insulinogenic index than patients without CR {0.47 (0.34-0.71) vs. 0.39 (0.27-0.56), $P = 0.049$ }. And fasting C-peptide was lower in patients with CR than in patients without CR {1.1 (0.8-1.4) vs. 1.3 (0.98-1.7), significant-

ly, $P = 0.049$). Increase of plasma glucose level was significantly attenuated during OGTT in patients with CR as compared with patients without CR. Glucose excursion was also significantly improved in patients with CR as compared with patients without CR $\{-7 (-34.5-12.75) \text{ mg/dl vs. } 17 (-15-32) \text{ mg/dl}, P = 0.004\}$.

Conclusions: Cardiac rehabilitation reduces glucose excursion during 75g OGTT.

LIPID EFFECTS OF SWITCHING FROM FIBRATE THERAPY TO THE PRESCRIPTION OMEGA-3 THERAPY, ICOSAPENT ETHYL, IN STATIN-TREATED PATIENTS: A RETROSPECTIVE CASE SERIES

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Institution/University: Private Practice

Introduction: Patients receiving statin therapy for dyslipidemia often require an additional agent to control triglyceride levels. Options for add-on therapy include fibrates and omega-3 fatty acids. This study was designed to evaluate the effects of switching add-on therapy from fenofibrate to icosapent ethyl (the ethyl ester of the omega-3 fatty acid, eicosapentaenoic acid) on patient lipid profiles.

Methods: This was a retrospective analysis of patient records from a private medical practice in Western New York. Statin-treated patients with dyslipidemia who had been treated with fenofibrate and later switched to icosapent ethyl were selected for analysis. Lipid profiles before and after the switch to icosapent ethyl were compared.

Results: The records of 5 patients were analyzed. All patients had hypertension and were overweight, male, and at high cardiovascular risk. After the switch (icosapent ethyl therapy duration of 3.9-5.8 months), triglyceride levels decreased in 4 patients, and low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and total cholesterol levels decreased in all patients. High-density lipoprotein levels increased in 4 patients. Icosapent ethyl was well tolerated.

Implications: Switching from fenofibrate to icosapent ethyl as add-on to a statin therapy may provide an option for patients whose lipid profiles are not at treatment goals with add-on fibrate therapy.

Keywords: *eicosapentaenoic acid, fenofibrate, hypertriglyceridemia, icosapent ethyl, low-density lipoprotein cholesterol, triglycerides*

URINE PHTHALATE METABOLITE LEVELS IN RELATION TO MAIN METABOLIC SYNDROME COMPONENTS – DYSLIPIDAEMIA, HYPERTENSION AND TYPE 2 DIABETES

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Human exposure to phthalates may be associated with adverse metabolic health outcomes. We have investigated urine samples of patients ($n = 170$) from metabolic outpatient department. Using standard metabolic syndrome criteria and used therapy criteria we have classified patients as dyslipidaemic ($n = 87$), hypertensive ($n = 96$) and type 2 diabetes ($n = 56$). The 24 hours samples were sampled in phthalate free bottles 15 metabolites of phthalates were evaluated in relation to creatinine excretion All were analysed with enzymatic cleavage of glucuronide using ultra-high-performance liquid chromatography-electrospray ionization tandem mass spectrometry in one laboratory with External Quality control. Four metabolites: (mono (3-carboxypropyl) phthalate, mono OH-, OXO-, ex- (mono 2-ethyl-5-hydroxyhexyl)phthalate) were significantly higher in diabetic versus non-diabetic patients using Mann-Whitney test ($P < 0.001$ $P < 0.002$ $P < 0.002$ $P < 0.005$). Great variability and asymmetrical distribution was seen in phthalate levels. No difference was found between hypertensive and non-hypertensive and dyslipidaemic and non-dyslipidaemic patients. Using multiple regression the result was the same without influence of age.

Conclusion: Urine levels of some phthalates are significantly higher in type 2 diabetes. Phthalate levels can be in causal relation to beta cell dysfunction but also it can be only a result of specific diabetes behavior (e.g. diet, skin care). Further investigation in relation will be performed in higher number of diabetic patients with possible division to specific subgroups according to type 2 diabetic clinical patients heterogeneity.

BISPHENOL A URINE LEVEL IN METABOLIC SYNDROME COMPONENTS

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The Impact of organic pollutant Bisphenol A is discussed in diabetes and in immune disorders. We have analyzed the urine bisphenol A/creatinine level in patients with metabolic syndrome components (n = 168) from metabolic department. Patients were classified as dyslipidaemic (n = 87), hypertensive (n = 96) and type 2 diabetes (n = 58).

Results: of Mann-Whitney test in µg/L using ultra-high-performance liquid chromatography)

Conclusion: Urine levels of bisphenol A are not significantly different in type 2 diabetes, hypertension a dyslipidaemia. The levels in hypertension and diabetes are higher near the significance. This estrogenic compound could be perhaps protective in these two diseases. Analysis on a larger sample will be performed.

DIETARY N-3 POLYUNSATURATED FATTY ACIDS MITIGATES FRUCTOSE INDUCED-METABOLIC SYNDROME AND ADIPOSE TISSUE OXIDATIVE STRESS IN WISTAR RATS

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Objectives: High intake of fructose is one of the risk factor for metabolic syndrome (MS). In the present study we investigated the effect of short chain n-3 PUFA (α-linolenic acid; ALA) present in vegetable oil and long chain n-3 PUFA (Docosahexanoic acid; DHA and Eicosapentanoic acid; EPA) present in fish oil on fructose-induced MS along with adipose tissue oxidative stress.

Materials and Methods: Weanling male Wistar rats (n = 48) were divided into four groups and fed with control-diet ST-200 (54.5% starch), FR- 200 (54.5% fructose), FR- 2 diet (54.5% fructose + α-ALA, n6/n3 = 2) and FR- 5 diet (54.5% fructose & EPA + DHA, n6/n3 = 5) for 3 months. Body composition was measured. Plasma fasting glucose, insulin, triglycerides and total cholesterol levels were measured. Insulin resistance was measured by homeostatic model assessment (HOMA) and glucose tolerance by oral glucose tolerance test. Lipid peroxidation (Thiobarbituric acid reactive substance) in adipose tissue was measured along with activities of antioxidant enzymes, glucose-6-phosphate dehydrogenase (G6PDH), glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase activities.

Results: High-fructose feeding for 3 months induced MS features including visceral adiposity, hypertriglyceridemia, hypercholesterolemia, insulin resistance and glucose intolerance in rats. ALA and DHA+EPA supplementation significantly reduced fructose-induced hypertriglyceridemia, hypercholesterolemia and glucose intolerance. HOMA-IR was significantly reduced by DHA+EPA supplementation, but not by ALA. ALA and DHA+EPA supplementation significantly decreased lipid peroxidation in adipose tissue along with G6PDH, Gpx and SOD activities without altering visceral obesity. Supplementation of n-3 PUFA did not alter visceral adiposity.

Conclusion: Here, we conclude that both ALA and DHA+EPA supplementation ameliorates fructose-induced hypertriglyceridemia, hypercholesterolemia, glucose intolerance and adipose tissue oxidative stress without altering visceral adiposity.

Key words: High fructose, Metabolic syndrome, Adipose tissue, PUFA.

PREECLAMPSIA RELATED TO UNTREATED GESTATIONAL DIABETES MELLITUS EPIGENETICALLY AFFECTED GENES INVOLVED IN INFLAMMATION

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Gestational diabetes mellitus (GDM) is a pathological state of carbohydrate intolerance during pregnancy, which when left untreated increases the risk of adverse pregnancy outcome like preeclampsia (PE). Underlying mechanism for GDM development is insulin resistance. Enough evidence suggests that inflammation is the central feature of insulin resistance. Thus we hypothesized that various epigenetic marks sensitive to environmental influence play an important role to the development of PE in poorly treated GDM with diminished insulin sensitivity. Our aim was to profile, in maternal serum samples, the association of altered methylation in genes corresponding to inflammation, in PE and GDM. Methylation levels were measured in 6 GDM, 6 PE and 6 healthy mothers (HV), matched for BMI (pre-pregnancy) and age, using the Human Inflammatory Response and Autoimmunity EpiTect Methyl II Signature PCR Array profiles. The microarrays validated with Q-PCR. GHBA1c levels were higher in PE than GDM ($P < 0,05$) ($5,67 \pm 0,2\%$ vs $4,93 \pm 0,3\%$) and HOMA-IR values were significantly higher in both diabetic groups than HV, but insignificantly different between them. Regarding GDM only ATF-2 gene and in PE ATF-2, IL13, IL15 and IL17RA appeared hypermethylated compared to HV. In GDM ATF2, CCL23, IL12B and IL6ST were found hypermethylated compared to PE. Genes CCL25, CXCL14, CXCL3, CXCL5, CXCL6, FADD, GATA3, IL12B, IL13RA, IL17C, IL6ST, IL7 and INHA were found hypomethylated only in both GDM and PE. Our results reveal that epigenetic effects on genes involved in the inflammatory process seem to play an important role in glucose intolerance and insulin insensitivity in GDM and PE.

ENDOCRINE DISRUPTOR – DDE AND DIFFERENTIATION OF ADIPOCYTES

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Purpose: White adipose tissue (WAT) represents a reservoir of persistent organochlorine pollutants (POPs). Epidemiological studies have revealed association between POPs exposure and risk of diabetes mellitus type 2. It is suggested that POPs may crossroad or modulate the effect of endogenous ligands of nuclear transcription factors, participating in differentiation, metabolism and the secretory function of adipocytes. These mechanisms include most importantly endocrine disrupting potency of POPs mixtures on androgen, estrogen or thyroid hormone metabolism/functions in WAT.

Material: To examine the effect of 2,2-bis (4-chlorophenyl)-1, 1-dichloroethene (DDE), still the most prevalent POPs in human WAT, on adipocyte differentiation and metabolism, we prepared an in vitro model of adipocytes from human mesenchymal stem cells derived from adipose tissue (hADMSC).

Methods: The ongoing process of differentiation was described by quantitative assessment of the expression of selected genes using RT real-time PCR with LNA probes. These genes are involved in the processes of implementing the undifferentiated phenotype of adipocytes - OCT4 (octamer-binding transcription factor 4), or direction of differentiation in adipocytes - PPAR γ (peroxisome proliferator-activated receptor- γ), and PPARGC1B (peroxisome proliferator-activated receptor gamma, coactivator 1 beta). We monitored DDE effect on insulin receptor pathway and lipid metabolism, by assessment of expression of genes: insulin receptor (INSR), homo sapiens v-akt murine thymoma viral oncogene homolog 2 (AKT2), sterol regulatory element-binding protein (SREBP-1), ATP citrate lyase (ACLY), hormone-sensitive lipase (LIPE) and fatty acid synthase (FASN).

Results and Conclusion: There were not found any statistical differences in expressions of genes mentioned above in DDE exposed and control hADMSCs during the process of their differentiation.

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ASSESSMENT OF THE GLUCOCARD® 01 COMPARED TO THE GLOBAL ACCURACY PERFORMANCE CRITERIA

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Background: Blood Glucose Monitoring Systems (BGMS) are an important monitoring tool to support the management of blood glucose levels for individuals with diabetes mellitus. The global BGMS accuracy performance criteria includes 95% of results within ± 15 mg/dL for glucose samples < 100 mg/dL and 95% of results within 15% of reference for glucose samples ≥ 100 mg/dL. In addition, 99% of the results need to fall within the A&B zones of the consensus error grid.

Objective: The purpose of this study was to demonstrate that the GLUCOCARD® 01 meets the global BGMS accuracy performance criteria.

Method: Three lots of GLUCOCARD® 01 test strips were analyzed for performance and bias comparison (n = 104 data points). Samples were collected from the fingertip of confirmed diabetic subjects by trained personnel. Reference values were obtained using the YSI Model 2300 Analyzer. Data was analyzed using the accuracy performance criteria of 95% of results within ±15 mg/dL for glucose samples <100 mg/dL and 95% of results within 15% for glucose samples ≥100 mg/dL.

Result: 100% of <100 mg/dL samples (n = 7/7) were within ± 15 mg/dL meeting the 95% accuracy criteria. 96.0% of the ≥100mg/dL samples (n = 93/97) fell within the pre-determined 15% meeting the 95% performance criteria. All data were within the A and B zones of the Consensus Error Grid. The overall bias was -1.8% and the correlation coefficient (r) 0.98. The data demonstrates a strong linear relationship between the YSI reference method and BGMS results.

Conclusion: GLUCOCARD® 01 meets the global accuracy performance criteria.

ACCURACY OF THE ASSURE® PRISM MULTI AS IT RELATES TO THE ISO 15197: 2013 REQUIREMENTS IN THE MONITORING OF DIABETES MELLITUS

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University: ARKRAY USA, Inc

Background: Blood Glucose Monitoring Systems (BGMS) are used to monitor and regulate blood glucose levels in diabetes mellitus. The gold standard in measuring the accuracy of BGMS is the ISO 15197:2013. System accuracy performance criteria are defined as 95% of BGMS values at <100 mg/dL must be within ±15mg/dL of the reference analyzer results, and for samples with glucose concentrations ≥100 mg/dL, 95% of BGMS values need to be within 15% of the reference analyzer results. In addition, 99% of all results are required to fall within A and B zones of the Consensus Error Grid.

Purpose: Demonstrate that the Assure® Prism multi meets the ISO 15197:2013 accuracy performance requirements.

Methods: Three lots of Assure® Prism multi blood glucose test strips were evaluated for performance and bias

comparison (n = 600 data points). Reference values were obtained using the YSI Model 2300 Analyzer. Data was analyzed using the minimum system accuracy performance criteria published in the ISO 15197:2013.

Results: 99.5% of the <100 mg/dL samples (191/192) were within ±15 mg/dL thus meeting the 95% accuracy criteria. 99.0% of the ≥100mg/dL samples (n = 403/408) fell within the pre-determined 15% which met the 95% performance criteria. All data were within the A and B zones of the Consensus Error Grid. Overall bias was 0.16% (average of all three lots) demonstrating strong agreement between the Assure Prism multi and YSI reference analyzer results. Good linear regression was demonstrated.

Conclusion: Data acquired on the Assure® Prism multi met the ISO 15197:2013 system accuracy performance criteria.

EVALUATION OF THE ONE-YEAR EFFICACY, SAFETY AND GLYCEMIC EFFECTS OF EVOLOCUMAB (AMG 145) IN 4,802 PATIENTS WITH, AT HIGH RISK FOR, OR AT LOW RISK FOR, DIABETES MELLITUS

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Introduction: We investigated the effects of the PCSK9 inhibitor evolocumab (AMG 145), a fully human monoclonal antibody to PCSK9, on glycaemia and adverse event (AE) rates in patients stratified by glycaemic status.

Methods: In two open-label trials (OSLER-1 and OSLER-2), 4,802 patients completed one of 13 phase 2 or 3 parent studies of evolocumab and were randomly assigned (2:1) to either evolocumab 140 mg every 2 weeks or 420 mg monthly plus standard of care (SoC) or SoC alone. Changes in fasting plasma glucose (FPG), HbA_{1c}, and AEs were evaluated over 48 weeks in three groups: 852 with type 2 diabetes mellitus (T2DM), 2,432 at high risk for T2DM (metabolic syndrome, IFG, HbA_{1c} >6% or BMI >30kg/m²), and 1,518 at low risk for T2DM.

Results: No notable differences were seen in median (SE) change in FPG from baseline to 48 weeks in patients on evolocumab + SOC compared with SoC alone (Figure).

Mean (SE) HbA_{1c} changes at week 48 in patients on evolocumab + SoC and in patients on SoC alone were +0.16 (0.05) and +0.23 (0.06)% in patients with diabetes; +0.05 (0.01) and +0.06 (0.01)% in patients at high diabetes risk; and +0.06 (0.01) and +0.07 (0.01)% in patients at low risk of diabetes. Rates of AEs (evolocumab + SoC vs. SoC alone) were: 64% and 63% (T2DM); 69% and 64% (high diabetes risk); and 69% and 63% (low diabetes risk).

Conclusion: Evolocumab showed encouraging safety with no measurable effect on glycaemic parameters despite reducing LDL-C levels markedly.

METABOLIC SYNDROME AND ATTAINMENT OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) GOALS IN THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) FROM 2003–2004 TO 2011–2012

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Background: Metabolic syndrome is an important risk factor for cardiovascular disease, so lifestyle changes and effective management of dyslipidemia are recommended. We used data from NHANES to estimate the prevalence of metabolic syndrome, as defined by NCEP ATP III, and dyslipidemia treatment patterns from 2003–2012.

Methods: The proportion of individuals with metabolic syndrome was calculated for each 2-year NHANES survey between 2003–2004 and 2011–2012. Proportions of individuals receiving lipid-modifying therapy (LMT) and achieving NCEP ATP III-recommended low-density lipoprotein cholesterol (LDL-C) levels of <100, <130, and <160 mg/dL for high-, intermediate-, and low-risk adults, respectively, were calculated and extrapolated to the US adult population.

Results: The estimated prevalence of metabolic syndrome was consistently around 50 million adults between 2003–2004 and 2011–2012. The proportion of these patients receiving LMT increased from 24% to 31% over this time; nevertheless, there did not appear to be any improvement in LDL-C goal attainment over the five surveys, with consis-

tently around 40% (17 million individuals) having LDL-C above the level recommended for their risk category. Goal attainment varied by NCEP ATP III risk category, but there appeared to be no consistent improvement in the number of patients attaining LDL-C goal for any of the risk categories between 2003–2004 and 2011–2012.

Conclusion: Despite a strong association between metabolic syndrome and cardiovascular disease and an increased use of LMT, dyslipidemia is undermanaged in this population. This highlights the need for more aggressive identification and treatment of at-risk individuals.

TREATMENT PATTERNS AND LDL-C GOAL ATTAINMENT IN PATIENTS WITH DIABETES: AN ANALYSIS OF TEMPORAL TRENDS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES)

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Background: Patients with diabetes, aged 40–75 years, are candidates for statin therapy according to 2013 ACC/AHA guidelines, with recommended statin intensity based on estimated 10-year cardiovascular risk. We estimated the prevalence of diabetes and statin treatment patterns over five 2-year periods (2003–2012) in US adults using NHANES data.

Methods: Prevalence of diabetes was determined in individuals in NHANES surveys between 2003–2004 and 2011–2012. Proportions of patients with diabetes receiving statins and achieving low-density lipoprotein (LDL-C) levels of <100 mg/dL in each survey were estimated and extrapolated to the US adult population.

Results: From 2003–2004 to 2011–2012, estimated prevalence of diabetes increased from 22.1 to 30.0 million adults. The proportion of patients with diabetes receiving statins increased from 35% (7.7M) to 45% (13.6M) over the same period. The percentage of individuals achieving LDL-C <100 mg/dL grew by 12% (38% to 50%; Figure). In each survey, ~9M patients with diabetes and LDL-C ≥100 mg/dL were not receiving lipid-lowering medication.

Combining data from all five surveys and extrapolating to the US population, there were consistently more men than women with diabetes (ratio 1.1 to 1.0), and a greater percentage of men, compared with women, achieved LDL-C <100 mg/dL (53% vs 41%). Conclusion This temporal trends analysis confirms that the prevalence of diabetes has increased by 8M from 2003–2004 to 2011–2012. Hypercholesterolemia tends to be undertreated in this high-risk population, particularly in women, with ~60% of women with diabetes (6.9M) not achieving LDL-C <100 mg/dL. [250 of 250 words]

EFFICACY OF ONE YEAR OF TREATMENT WITH THE PCSK9 INHIBITOR EVOLOCUMAB (AMG 145) IN 4,802 PATIENTS WITH OR WITHOUT TYPE 2 DIABETES

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Introduction: In a pooled analysis of patients with type 2 diabetes mellitus (T2DM) from 2 open-label extension trials, we evaluated the efficacy of one year of subcutaneous evolocumab treatment added to standard of care (SoC) in patients with or without T2DM at baseline.

Methods: In total, 4,802 patients completed one of 13 phase 2 or 3 studies and continued into OSLER-1 (phase 2 extension) or OSLER-2 (phase 3 extension). Patients were randomly assigned 2:1 to either evolocumab 140 mg every 2 weeks or 420 mg monthly plus SoC or SoC alone. Changes in LDL-C (calculated) and other lipids were evaluated at week 48 in patients with or without T2DM. LDL-C changes within T2DM subgroups were also evaluated.

Results: In total, 563 patients with and 2,637 without T2DM (defined by history, glycemic criteria, or baseline diabetes medication) received evolocumab plus SoC in the open-label extension phase; 289 and 1,313, respectively, received SoC alone. In patients on evolocumab plus SoC, mean percent changes in LDL-C from baseline versus SoC at one year were -60% and -58% in those with and without T2DM, respectively. Similar changes in LDL-C were

observed between treatment arms in T2DM subgroups (Figure). Beneficial changes were also observed in other lipids.

Conclusion: One year of treatment with evolocumab resulted in marked and comparable reductions in LDL-C in patients with and without T2DM, and these changes were similar across T2DM subgroups, irrespective of baseline characteristics.

PXL770 DEMONSTRATES THERAPEUTIC POTENTIAL AS A NEW DIRECT AMP KINASE ACTIVATOR

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AMPK is a heterotrimeric kinase playing a major role in regulating cellular energy balance. AMPK has raised widespread interest as a potential therapeutic target for metabolic diseases. Direct AMPK activation is expected to decrease insulin resistance, lipid disorders and to improve glycemic control. PXL770 is a small molecule, shown to directly activate all AMPK holoenzymes tested, with a higher potency for b1-containing isoforms. PXL770 activates AMPK allosterically and protects AMPK against dephosphorylation, as demonstrated in several recombinant AMPK isoforms. PXL770 binds to AMPK differently from the natural AMPK ligand, AMP, and its binding site involves the CBM region in the b subunit. Cell-based assay confirmed that PXL770 inhibits hepatic de novo lipogenesis in an AMPK-dependent manner. PXL770 exhibits good oral availability and dose linear pharmacokinetic profile. In an obese type 2 diabetic rodent model (ob/ob mice), orally administered PXL770 during 6 weeks significantly and dose dependently improves glucose tolerance without an increase in insulin levels suggesting an insulin sensitizing effect. PXL770 significantly improved HbA1c, decreased plasma triglycerides as well as liver weight and triglycerides content showing an improvement in liver steatosis. In the same model, we showed that PXL770 induced a significant increase of Phosphorylated AMPK levels in both liver and muscle, demonstrating in vivo target engagement. In conclusion, PXL770 is a novel direct AMPK activator that improves both glycemic control and lipid profile, the two main cardiovascular risk factors, and potentially could be a new oral agent for the treatment of Type 2 diabetes and dyslipidemia.

ASSOCIATIONS BETWEEN SLEEP DURATION AND HYPERINSULINEMIA AMONG EUGLYCEMIC U.S. ADULTS: NHANES 2007-2010

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Evidence suggests a strong and independent relationship between fasting hyperinsulinemia and cardiometabolic risk. However, few population-based studies have examined the deleterious associations between short and long sleep duration and hyperinsulinemia.

Purpose: Examine the associations between sleep duration and hyperinsulinemia in a nationally representative sample of euglycemic U.S. adults.

Methods: Study sample included adult (≥ 20 years of age) participants ($n = 2,763$) in the 2007-2010 National Health and Nutrition Examination Survey. Sleep duration was categorized as short (≤ 6 h), adequate (7-8 h) or long (≥ 9 h). Hyperinsulinemia was defined as the 75th percentile of fasting insulin in the background population. Logistic regression analysis was used to examine the associations between sleep duration and hyperinsulinemia. Logistic regression models were adjusted for age, gender, race, education, sedentary activity, and waist circumference.

Results: Analysis revealed significantly higher odds of hyperinsulinemia in adults reporting ≤ 6 h of sleep (OR 1.46; 95% CI 1.01-2.10, $P = 0.044$) when compared to the referent group reporting 7-8 h of sleep. This association was attenuated following adjustment for waist circumference (OR 1.24; 95% CI 0.86-1.78, $P = 0.236$). Conclusion: Short sleep duration was significantly associated with hyperinsulinemia in euglycemic U.S. adults. This deleterious relationship may be mediated by central adiposity.

PARASYMPATHETIC NERVOUS SYSTEM MODULATES GLUCOSE HOMEOSTASIS IN RESTRICTED MICE FED ON A HIGH FAT DIET

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Protein malnutrition, lead to an increased risk for chron-

ic diseases, such as obesity and type 2 diabetes. Studies suggest that parasympathetic nervous system (PNS) can participate of this process. Therefore, herein we evaluated the PNS contribution to obesity development and glucose homeostasis impairment in mice fed with low protein followed by a high fat diet. Weaned 30-day C57Bl/6 mice were submitted to a low protein diet (6% protein - R). After 4 weeks, R group was divided into R, RH that started to receive a HFD and RHVag that underwent vagotomy, and was kept receiving the HFD. Corporal parameters, glucose tolerance, insulin secretion and sensitivity, and hepatic insulin-degrading enzyme (IDE) expression were evaluated. RH group displayed an increased in body weight and fat deposits, hyperglycemia, glucose intolerance, and insulin resistance compared to R group. In addition, Akt phosphorylation (pAkt) was lower in gastrocnemius muscle, liver and adipose tissue whereas glucose-induced insulin secretion was higher than R mice. Vagotomy did not alter body weight, fats pads and insulin resistance observed by KITT and pAkt, however, improved glucose tolerance. RHVag showed reduced insulin secretion in response to high doses of glucose, but presented higher insulinemia 15 min after glucose load. The IDE hepatic expression was higher in RH mice compared with R, and vagotomy normalized this protein expression in RHVag animals. In conclusion, vagotomy in malnourished animals exposed to HFD improved glucose homeostasis. PNS may modulate IDE expression lowering insulin clearance to maintain glycemia by reducing insulin disposal from the plasma.

This study was approved by the Institution's Committee for Ethics in Animal Use (CEUA/IB/Unicamp, protocol 3379-1)

LIPOPROTEIN ASSOCIATED PHOSPHOLIPASE A2: A SURROGATE MARKER OF CORONARY ARTERY DISEASE IN DIABETIC PATIENTS

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Background: Lipoprotein-associated phospholipase A2 [Lppla2] is known as an emerging marker of coronary artery disease (CAD). However its role and levels have not been documented clearly in diabetic patients with CAD in Indians. The aim of this study was to explore if Lppla2 can be established as a surrogate marker of CAD in diabetic patients and compare it with other established markers like hs-CRP. Method: Sixty individuals with angiographically proven CAD and 30 healthy individuals matched for age

& sex were studied. CAD patients were divided into two groups based on presence (n = 30) [Group I] and absence (n = 30) [group II] of type 2 diabetes mellitus (DM). The serum levels of Lppla2, hs-CRP were measured by ELISA. Angiographic clinical vessel scoring was also done for all the patients. Results: Both groups of CAD with and without DM had significantly higher levels of Lppla2 (Group I-408.48 +/- 38.96 ng/ml, Group II 272.88 +/-34.21ng/ml respectively) and hscrp (Group I-10.61 +/- 1.34 mg/l, Group II-5.75 +/-2.59 mg/l respectively) when compared with healthy control subjects (Lppla2 = 200.82 +/-20.97ng/ml & hscrp = 1.89 +/-1.34mg/l) [$P<0.001$]. Lppla2 levels between the two CAD groups were highly significant ($P<0.001$), levels being maximum for CAD with type 2 diabetes (Group I) which could be due an increase in its substrate sldl and oxidised LDL in DM. Angiographic clinical vessel score of CAD severity was also higher in CAD with DM. Lppla2 levels correlated strongly ($r = 0.763$, $P<0.001$) with the angiographic clinical vessel score in diabetes patients with CAD while hscrp has moderate correlation with the vessel score ($r = 0.475$, $P<0.01$).

Conclusion: Lppla2 and hscrp elevation is increased with patients of type 2 diabetes mellitus with CAD as compared to only CAD patients and Lppla2 levels increase with the severity of CAD in diabetes patients. Measurement of Lppla2 may be considered as a surrogate marker for better prediction of cardiovascular risk in diabetes patients.

EARLY CLINICAL EXPERIENCE OF DUODENAL MUCOSAL RESURFACING (DMR), A NEW ENDOSCOPIC APPROACH TO TREATING TYPE 2 DIABETES (T2D)

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Introduction: Bariatric surgery improves glycemia in T2D. Exclusion of nutrient contact with an abnormal duodenal surface may be a key mechanistic contributor, involving potential weight-independent changes in insulin sensitivity. DMR, a non-invasive, upper endoscopic procedure involving thermal ablation of the duodenal mucosa, also appears to elicit glycemic improvements in T2D. We report the first-in-human clinical experience with DMR.

Objectives: Assess procedural safety and glycemic measures for 6 months after a single DMR procedure in patients with T2D and hba1c >7.5% on at least 1 oral anti-diabetic agent. Methods: Using novel balloon catheters, DMR was conducted on varying lengths of duodenum in anesthetized patients at a single center (Santiago, Chile).

Results: A total of 39 patients were treated (baseline hba1c: 9.5%): 28 had ablation of a long-duodenal segment (LS-DMR; ~9.3 cm treated) and 11 had short-segment ablation (SS-DMR; ~3.4 cm treated). Baseline hba1c was reduced by 1.2% at 6 months in the full cohort. More potent glycemic effects were observed among the LS-DMR cohort, who experienced a 2.5% reduction in baseline mean hba1c at 3 months post-procedure vs 1.2% with SS-DMR ($P<0.05$). Excluding patients who reduced concomitant anti-diabetic medication post-procedure, LS-DMR among patients with a baseline hba1c of 7.5-10% (n = 8) lowered hba1c from a mean of 8.8% to 7.1% at 6 months ($P<0.05$), accompanied by a modest weight reduction of 2.3 kg. Overall, DMR was well tolerated with minimal gastrointestinal symptoms post-procedure. Three patients experienced duodenal stenosis treated successfully by balloon dilation.

Conclusions: To date, single procedure DMR elicits a robust improvement in glycemia in T2D with acceptable safety and tolerability. Further examination of safety, efficacy, durability and possible mechanisms is needed.

THE INFLUENCE OF SLEEP DURATION ON ADIPOKINES LEVELS AND CARDIO-METABOLIC RISK FACTORS AMONG SCHOOL-AGE CHILDREN IN BEIJING: DATA FROM BCAMS STUDY

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Objectives: To assess the influence of sleep duration on adipokines and metabolic disorders among Chinese school-children. Methods: Total of 3466 children aged 6-18 years old were derived from the Beijing Child and Adolescent Metabolic Syndrome study (BCMAS). Characteristics of metabolic syndrome components and insulin resistance were evaluated. Adipokines including leptin, total and high molecular weight (HMW) adiponectin, resistin, FGF21 and RBP-4 were measured by ELISAs. Sleep duration, physical activity and dietary habits were assessed by questionnaire.

Results: For the children aged 6-12 years, shorter sleep duration was significantly associated with increased BMI, waist and fat percentage, higher fasting glucose, insulin and

HOMA-IR, and higher triglyceride and lower HDL-C, and higher leptin, FGF21 and lower total and HMW adiponectin levels. After adjusted for age, gender and obesity, the associations between sleep duration and glucose, HOMA-IR remained significantly; and each hour reduction in sleep time was associated with a 0.077 increase in ln-leptin ($P = 0.002$), a 0.118 increase in ln-leptin/ HMW-adiponectin ratio ($P < 0.001$) and a 0.038 decrease in ln-HMW-adiponectin ($P < 0.05$). However, among the 13-18 years old group, shorter sleep duration was significantly associated with increased waist and fat percentage, and only association between RBP-4 and sleep duration ($P = 0.05$) was observed after adjustment. Conclusions: The sleep duration has a central influence on obesity, insulin resistance and glucose metabolism among children, especially in the younger, and adipokines dysregulation may play an important role in it. Further investigation of the effect of sleep on adipose tissue function should be pursued.

INSULIN RESISTANCE, OBESITY AND SKELETAL MUSCLE IN A YOUNG NON-DIABETIC POPULATION CLINICAL AND BASIC ASPECTS

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Objectives: This study investigated whether there's an association between lower insulin sensitivity (LIS) and muscle cross-sectional area (CSA) & handgrip force in a healthy adult male population, and whether this association is mediated by obesity. Furthermore, potential influence of anabolic and catabolic parameters are explored.

Methods: 358 healthy young men were divided into a LIS group and a more insulin sensitive group, based on upper and lower quartile of HOMA-IR. Muscle density, muscle CSA, handgrip force, creatinine, vitamin25(OH)D, leptin, sex hormone binding globuline (SHBG), total, free & bio-available testosterone (TT, FT, bio-av T), and total, free & bio-available estradiol (TE2, FE2, bio-av E2) levels were

compared between these groups, adding age, physical activity and additionally whole body fat mass as covariates.

Results and Conclusions: In healthy subjects, LIS is associated with lower relative handgrip force and lower vitamin25(OH)D levels, both independent of overall obesity. LIS subjects have higher muscle CSA in lower leg, higher urinary creatinine, lower muscle density, lower levels of FT, bio-av T, & leptin, but these differences disappeared after correction for fat mass. They have higher forearm muscle CSA and lower levels of TT & SHBG, all mediated by obesity, but remaining significantly different after fatmass-correction. TE2 became significantly lower in LIS-subjects because of this fatmass-correction. Urinary creatinine, testosterone, vitamin 25(OH)D or leptin do not seem to play a role in the lower relative handgrip force in LIS subjects, but muscle density, muscle CSA, serum creatinine, SHBG, TE2, FE2, & bio-av E2 seem to do so.

COMPARATIVE ANALYSIS OF HYPOGLYCEMIC PROPERTIES OF AQUEOUS LEAF EXTRACT OF VISCUM ALBUM (MISTLETOE) AND RHIZOMA ANEMARRHENAE EXTRACT IN THE MANAGEMENT OF ALLOXAN - INDUCED DIABETES MELLITUS

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University: Olabisi Onabanjo University

Introduction: This study was aimed at comparing the efficacy of leaf extract of *Viscum album* (Mistletoe) with that of *Rhizoma anemarrhenae* in the management of type II diabetes mellitus.

Materials and Methods: 36 albino wistar rats weighing 180 - 230g were randomly divided into 6 groups of 6 rats each, thus; Group 1 - control; group 2 - diabetic untreated group; group 3 - diabetic group, treated with 0.5 ml/100g *Rhizoma anemarrhenae*; group 4 - diabetic group, treated with 120 mg/kg mistletoe leaf extract; group 5 - control animals, treated with 0.5 ml/100g *Rhizoma anemarrhenae*; group 6 - control animals, treated with 120 mg/kg mistletoe leaf extract. Administration of extracts was done per oral route and lasted for 21 days. Also, the pancreatic tissue sections were observed with transmission electron micrographs.

Results: Mistletoe treated diabetic group had a significantly ($P < 0.001$) lower fasting blood glucose (FBG) level compared to diabetic untreated group. *Rhizoma anemarrhenae* treated diabetic group had a significantly ($P < 0.001$) lower FBG level compared to mistletoe treated diabetic group. *Rhizoma anemarrhenae* treated diabetic group had

a significantly ($P < 0.05$) lower mean daily food and water intake compared to mistletoe treated diabetic group. Rhizoma anemarrhenae treated diabetic group had a significantly ($P < 0.001$) higher body weight compared to mistletoe treated diabetic group. The Rhizoma anemarrhenae treated control group had a significantly ($P < 0.001$) higher body weight compared to mistletoe treated control group.

Conclusion: Based on the outcome of this study, it can be inferred that Rhizoma anemarrhenae proved to be more beneficial in the management of type II DM compared to mistletoe leaf extract.

LEPTIN IS A POTENTIAL MEDIATOR OF PHYSIOLOGIC INSULIN RESISTANCE IN PUBERTY

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Puberty is associated with a progressive but transient physiologic insulin resistance, perhaps due to increased growth hormone secretion. Furthermore, obese youth are at risk for becoming metabolically unhealthy and developing type 2 diabetes during puberty, although mechanisms are unclear. Therefore, understanding potential mediators of insulin sensitivity (Si) during puberty is critical.

Methods: Lean ($n = 44$) and obese ($n = 46$) early pubertal (Tanner 2-3) youth had Si evaluated by IV glucose tolerance testing (IVGTT). Univariate regression assessed potential predictors of Si early in puberty, adjusting for sex, race, Tanner stage and BMI z-score. Variables assessed included: lipids, dehydroepiandrosterone-sulfate, estradiol, total testosterone, adiponectin, leptin, insulin growth factor-1 (IGF-1), waist circumference (WC), % body fat (by DXA), and free androgen index. Stepwise selection identified factors that best predict Si.

Results: Leptin ($R^2 = 0.65$, $P = 0.0032$), IGF-1 ($R^2 = 0.56$, $P = 0.004$) and WC ($R^2 = 0.60$, $P = 0.0002$) were all significant predictors of Si in univariate analyses. Using stepwise selection, IGF-1 ($P = 0.03$), race/ethnicity ($P = 0.003$), and leptin ($P < 0.0001$) remained independent predictors of Si.

Conclusions: Factors controlling Si during puberty are complex and may be only partly regulated by growth hor-

mone. Specifically, leptin may also play a role in reduced pubertal Si, independent of body fat. Because leptin changes differently in girls and boys as puberty progresses, studies evaluating metabolic effects of puberty need to strongly consider sex differences.

ACUTE EFFECT OF WASABI (WASABIA JAPONICA) ON BODY COMPOSITION OF WISTAR RATS WITH OBESITY AND RELATED DISEASE

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University: The University of Queensland

The prevalence of obesity is growing rapidly in the western population. Over the past decade studies have associated obesity with metabolic dysfunction and low-degree systemic inflammation. Plant sourced foods such as wasabi have demonstrated to be an effective therapeutic component against inflammation, obesity and chronic diseases. Wasabi (*Wasabia japonica*) is a member of the Brassicaceae family and its main active constituents have been identified as isothiocyanates such as allylisothiocyanate (AIT) and 6-Methylsulfinylhexyl isothiocyanate (6-MSITC). AIT has several biological functions including anti-carcinogenic, anti-inflammatory, antimicrobial and antiplatelet aggregation. Recent studies have shown that wasabi consumption improves β -oxidation of fatty acids and suppresses ACC and FAS enzymes, as well as C/EBP α , PPAR γ and SREBP-1c expression. The present study aims to elucidate the influence of Wasabi Japonica on body composition in high-fat high-carbohydrate (HFHC) diet-induced obese rats. Rats were fed either a corn starch (CS) or high-fat high-carbohydrate (HFHC) diet for 8 weeks. After this period, CS rats ($n = 12$ /group) and HFHC rats ($n = 12$ /group) were treated with 5% of Wasabia Japonica (rhizome and steam blend) for 3 weeks. Body composition markers such body weight and abdominal circumference had a significant decrease during the studied period. Predominantly, the HFHC group had a reduction of approximately 12% of body weight whereas the CS group had a decrease of 5%. In this 3-week trial, wasabi treatment resulted in a clinically significant loss of body weight compared with placebo, providing evidence to support a novel alternative therapy to assist in the management of obesity and related diseases.

ADIPONECTIN: LEPTIN RATIO AND METABOLIC SYNDROME IN NORTH INDIAN POSTMENOPAUSAL WOMEN

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Background: Adiponectin and leptin are pro insulin and play a protective role in metabolic syndrome. However increase adiposity lead to leptin resistance also contributes to high circulating leptin may cause increase risk for metabolic syndrome.

Methods: In the present cross sectional case-control study of 523 postmenopausal women were enrolled out of which 270 postmenopausal women with metabolic syndrome according to NCEPATP guidelines and 253 healthy control postmenopausal women without metabolic syndrome. Anthropometrical measurements, lipid profile, glucose estimation were done and insulin, adiponectin and leptin level were determined by ELISA.

Results: Waist circumference, waist-to-hip ratio, body mass index, lipid profile (TC, TG, VLDL, LDL, TC/HDL & HDL/LDL), glucose, insulin, IR, serum leptin level and L:A ratio were observed significantly higher ($P < 0.001$) while HDL, LDL/HDL and serum adiponectin level were observed significantly lower in study group as compare to control group. Furthermore, adiponectin and leptin ratio was positively correlated with HDL/ LDL ratio and adiponectin level and negatively correlated anthropometric measurements, TC, LDL, TC/ HDL, LDL/ HDL, insulin, IR and adiponectin level in postmenopausal women with metabolic syndrome.

Conclusions: Adiponectin and leptin ratio may play a protective role in the development of metabolic syndrome in post menopausal women.

Keywords: Postmenopausal women, Metabolic syndrome, L:A ratio, Waist circumference, glucose

CIRCULATING LEVELS OF TUMOR NECROSIS FACTOR- α AND INTERLEUKIN-6 IN CAD PATIENTS OF NORTH INDIAN POPULATION

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Background: Coronary artery disease (CAD) is considered as a variant of atherosclerosis. Tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6) are among the sensitive markers of systemic inflammation. The aim of this study was to evaluate the circulating levels of the cytokines; TNF- α and IL-6 in CAD patients.

Methods: Serum concentrations of TNF- α and IL-6 were measured in 54 patients with CAD (43 males & 9 female), and results were compared with age and sex-matched controls (38) without CAD. TNF- α and IL-6 concentrations in blood were assessed by enzyme-linked immunosorbent assay (ELISA).

Results: Baseline characteristics of the two groups were similar. TNF- and IL-6 levels were significantly higher in CAD group than controls ($P < 0.05$).

Conclusion: CAD patients showed increases in TNF- α and IL-6 levels compared to the controls. This study provides evidence for alterations in the proinflammatory cytokines which suggest the involvement of the immune system in the pathophysiology of CAD. Further studies are needed to evaluate the clinical significance of this increase in TNF- α and IL-6 levels. Keywords:- CAD, TNF- α , IL-6, Cytokines and Inflammatory.

COMBINATION WITH RED GINSENG AND POLYGONI MULTIFLORI AMELIORATES HIGH-FRUCTOSE DIET INDUCED METABOLIC SYNDROME

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Metabolic syndrome such as dyslipidemia, hypertension, obesity, impaired glucose tolerance and fatty liver, can be

caused by modification of diet by means of overconsumption of high fructose diet. This study was designed to investigate whether combination with Red ginseng and *Polygoni Multiflori Radix* (RGPM), widely used traditional herbal medicine, ameliorates on high fructose (HF) diet-induced metabolic syndrome. SD rats were fed the 60% HF diet with/without rosiglitazone, and RGPM 100, 300 mg/kg/day, respectively. RGPM or rosiglitazone groups initially received HF diet along 8 weeks, and supplementation with RGPM or rosiglitazone occurring during final 6 weeks. Chronic treatment with RGPM significantly decreased body weight, fat weight and adipocyte size. RGPM significantly prevented the development of the metabolic disturbances such as hypertension, hyperlipidemia and impaired glucose tolerance. RGPM also led to increase in high density lipoprotein level in the HF group. RGPM suppressed high-fructose diet induced vascular inflammation marker expression such as adhesion molecules and ET-1 in aorta as well as increasing of C-reactive protein (CRP) levels in plasma. Similarly, RGPM attenuated hepatic lipid accumulation by inhibition of monocyte chemoattractant protein-1 (MCP-1) expression. In conclusion, RGPM may be a beneficial therapy for the treatment of metabolic syndrome through the improvement of hypertension, obesity, hyperlipidemia, vascular inflammation and insulin resistance.

Keywords: Red ginseng; *Polygoni Multiflori Radix*; metabolic syndrome; vascular inflammation; stetohepatitis

BLACKCURRANT (*RIBES NIGRUM L.*) SUPPRESSES METABOLIC SYNDROME INDUCED BY HIGH-FRUCTOSE DIET IN RATS

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Increased fructose ingestion has been linked to obesity, hyperglycemia, dyslipidemia, and hypertension associated with metabolic syndrome. Blackcurrant (*Ribes nigrum*; BC) is a horticultural crop in Europe. To induce metabolic syndrome, Sprague-Dawley rats were fed a 60% high-fructose diet. Treatment with BC (100 or 300 mg/kg/day for 8 weeks) significantly suppressed increased liver weight, epididymal fat weight, c-reactive protein (CRP), total bilirubin,

leptin, and insulin in rats with induced metabolic syndrome. BC markedly prevented increased adipocyte size and hepatic triglyceride accumulation in rats with induced metabolic syndrome. BC suppressed oral glucose tolerance and protein expression of insulin receptor substrate-1 (IRS-1) and phosphorylated AMP-activated protein kinase (P-AMPK) in muscle. BC significantly suppressed plasma total cholesterol, triglyceride, and LDL content. BC suppressed endothelial dysfunction by inducing down-regulation of endothelin-1 and adhesion molecules in the aorta. Vascular relaxation of thoracic aortic rings by sodium nitroprusside and acetylcholine were improved by BC. The present study provides evidence of the potential protective effect of BC against metabolic syndrome by demonstrating improvements in dyslipidemia, hypertension, insulin resistance, and obesity *in vivo*.

Keywords: Blackcurrant; high-fructose; hypertension; obesity; diabetes

RAPID-ACTING INSULIN (RAI) PERSISTENCE AND CLINICAL OUTCOMES AMONG ELDERLY PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) NEWLY ADDING RAI TO BASAL INSULIN (BI)

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American Diabetes Association guidelines recommend adding a RAI to BI treatment in patients with T2DM and without adequate glycemic control in order to improve glycemic control. Here we describe how RAI persistence affects clinical outcomes in real-world practice settings. The study population comprised elderly Medicare beneficiaries (aged ≥ 65 years) who: initiated a RAI between July 2007 and December 2011; had continuous enrollment during the 6-month baseline and 12-month follow-up periods; and had >2 prescriptions for BI during baseline. Associations between RAI persistence (defined as 90-day gaps between RAI prescriptions) and change in A1C and severe hypoglycemia (any inpatient or emergency hypoglycemic episode during the 1-year follow-up period) were analyzed using multivariable analysis (ordinary least squares and logistic regressions). Observed selection bias in RAI persistence was controlled with Inverse Probability Treatment Weights (IPTW). Among 4,979 included patients (53.5% female, 78.3% White, 29.2% ≥ 75 years or older, mean A1C [available for $n = 1,792$] 8.6%, 59.4% A1C $>8\%$, 56.9% from the South, 36.9% enrolled in a Health Maintenance Organization), 3,927 had ≥ 2 RAI prescriptions, of whom

only 21% were persistent. After adjusting with IPTW, persistent RAI users had significantly higher A1C reduction as compared with non-persistent users (beta: -0.27 , $P < 0.05$). Persistence was not significantly associated with severe hypoglycemia (incidence 8.1%; a OR, 95% CI: 0.75, 0.56–1.01). Poor RAI persistence was observed among elderly patients with T2DM on BI. Improving RAI persistence among elderly patients with T2DM could enhance treatment effectiveness without increasing the risk for severe hypoglycemia.

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Disclosure Statements: Zhou, Fan, and Boss: employees of Sanofi US, Inc.

BISPHENOL-A INCREASES ARTERIAL BLOOD PRESSURE AND INDUCES REMODELING OF CORONARY ARTERIES IN MICE

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Background and Aim: Bisphenol-A (BPA) is an endocrine disruptor associated with higher risk of type 2 diabetes (T2D), insulin resistance and cardiovascular diseases (CVD). Similarly, protein-restricted diet predispose to T2D and CVD. We aimed to analyze BPA effects on arterial and left ventricular (LV) pressure, and cardiac structure of normal and protein-restricted mice.

Methods: Post-weaned Swiss male mice were fed with 14% (normoprotein diet, NP) or 6% (low protein diet, LP) protein diet during 8 weeks. Animals were treated subcutaneous with vehicle or BPA (50 $\mu\text{g}/\text{Kg}/\text{day}$) during the last 9 days. Arterial and LV hemodynamic and LV histologic analyses were performed.

Results: LP, BPA, and LP+BPA mice exhibited increased systolic arterial pressure (SAP: NP=100 \pm 3; BPA=121 \pm 5; LP = 133 \pm 9; LP + BPA = 137 \pm 4 mmHg); however, diastolic arterial pressure (DAP) and heart rate (HR) were increased only in LP + BPA-treated group (HR: NP = 191 \pm 14; BPA = 214 \pm 15; LP = 208 \pm 28; LPB + PA = 328 \pm 39

bpm). Both LV systolic pressure and maximal dP/dt were enhanced in LP + BPA mice. Cardiomyocyte diameter was similar among groups. LP, BPA, and LP + BPA mice exhibited increased coronary arteries thickness and wall/lumen (NP = 0.18 \pm 0.02; BPA = 0.29 \pm 0.01; LP = 0.26 \pm 0.03; LP + BPA = 0.27 \pm 0.02).

Conclusion: BPA treatment induced hypertrophic remodeling of coronary arteries and increased SAP in normal mice. In addition, LP + BPA exacerbated injury to cardiovascular system by enhancing HR, DAP and LV pressure. These changes might contribute to development of CVD in response to BPA and malnourishment. Acknowledgements: This work was supported by FAPESP CEPID-OCRC.

SIMVASTATIN REDUCES ER STRESS MARKERS AND AMELIORATES INSULIN SECRETION IN ISLETS FROM HYPERCHOLESTEROLEMIC MICE

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Background And Aims: Lipid accumulation are associated with the development of endoplasmic reticulum (ER) stress, resulting in a reduction of β cell mass and function. Based on this, the aim of this study was evaluate whether alterations in islets cholesterol content affects ER stress markers expression.

Methods: Males wild-type (WT) and low-density lipoprotein receptor knockout (LDLr^{-/-}) mice, 4 months of age, were fed with a chow-diet and received Simvastatin (Simv) (40mg/Kg) or Vehicle (carboxymethyl-cellulose 0.5%) by oral gavage, during 30 days. Glucose homeostasis was analyzed using oral glucose tolerance test (oGTT) (1.5g/kg BW); islets were isolated and used for measurements of glucose stimulated insulin secretion (GSIS); cholesterol content and protein expression (BIP, XBP1s, pPERK).

Results: LDLr^{-/-} showed a higher expression of ER markers (BIP, pPERK and XBP1s) compared to WT mice. Simvastatin treatment did not change the glucose tolerance. Islet cholesterol content was reduced (3,96 \pm 0,25 vs 2,99 \pm 0,10, $P < 0.05$) and the GSIS was increased by Simvastatin (1,65 \pm 0,15 vs 2,06 \pm 0,19, $P < 0.05$, LDLr^{-/-} vs LDLr^{-/-} Simv respectively). Also, the ER stress markers BIP and s-XBP1 were reduced by Simvastatin treatment.

Conclusion: The excess of cholesterol in LDLr^{-/-} male mice induces ER stress. Reduction of cholesterol leads to

an improvement on insulin secretion and this can be in part explained by reduction in ER stress.

MODELING GLYCEROL DYNAMICS FOLLOWING AN ORAL GLUCOSE CHALLENGE

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Insulin resistance (IR) is crucial in the pathology of the metabolic syndrome, which now affects more than a third of our population. Adipose tissue resistance to the suppressive effects of insulin on lipolysis may allow for excess free fatty acid delivery to both the liver and vasculature, contributing to fatty liver disease and cardiovascular disease. Whereas maximal adipose insulin sensitivity can be assessed with isotopic tracers during a hyperinsulinemic-euglycemic clamp, measurement of the lipolytic response to endogenous insulin secretion during an oral challenge is more complex. Using a constant infusion protocol with a glycerol tracer, we measured plasma glycerol and insulin concentrations in four adolescent girls during an oral challenge. To relate glycerol and insulin secretory dynamics and to establish a methodology for quantifying adipose IR in the fed state, we developed a differential-equations-based model of glycerol and insulin dynamics during an oral challenge. The proposed model describes explicit insulin action on glycerol suppression and captures the glycerol/insulin dynamics observed during the oral challenge. Moreover, model parameters provide a novel measure of adipose insulin sensitivity that will facilitate quantification of adipose IR in a clinical setting. This method can be simultaneously combined with other tracers to assess endogenous glucose production or release of pancreatic hormones such as GLP-1 to better understand tissue-specificity of IR and to identify potential mechanisms for IR that may provide targets for novel therapeutic approaches. Acknowledgements: The authors would like to thank the volunteers and their families for their participation in the study. This work was supported by the following grants: CDB: NSF DMS 1412571; MCG and CDB: Children's Hospital Colorado/Colorado School of Mines Collaborative Pilot Award; MCG: BIRCWH K12-HD057022; NORC P30 DK048520; UL1 TR001082; Boettcher Foundation Boettcher Webb Waring award; University of Colorado, Anschutz: Adult GCRC NIH Grant #M01-RR00051, Pediatric CTSC NIH Grant

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IMPROVEMENTS IN HOMA-IR AND ATHEROGENIC DYSLIPIDEMIA BY A COMBINATION OF 10% LOSS OF BODY WEIGHT AND PRESCRIPTION EICOSAPENTAENOIC ACID (ICOSAPENT ETHYL) IN A PATIENT WITH DIABETES MELLITUS AND STATIN INTOLERANCE

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Background: Patients with diabetes mellitus have an increased prevalence of atherogenic dyslipidemia and cardiovascular risk (CVR). Insulin resistance has also been associated with increased CVR. Statins are recommended to reduce CVR, but the management of patients who refuse statin therapy can be challenging. Refusal may be based on perceived or actual statin intolerance. Further, statins may not improve insulin resistance (IR). Case Presentation: We review the impact of initiating a highly purified prescription EPA, icosapent ethyl 4 g/day, along with 10% loss of body weight, on a 63-year-old obese male patient with hypertension, type II diabetes mellitus, atherogenic dyslipidemia, IR, and statin intolerance. He was on a stable diet, exercise regimen, and stable dose of medications for the duration of this report. Lipids, lipoproteins, and parameters related to diabetes mellitus and IR were evaluated before and 3 months after initiating icosapent ethyl (Table). During this period, he was able to lose 10% of his body weight (BMI decreased from 31.9 to 28.6) and he experienced improvements in fasting insulin levels (from 20 to 4 μ U/mL), HOMA-IR (from 6.5 to 0.9), glucose (from 130 to 93 mg/dL), and A₁C (from 7.2% to 5.2%) *% of total fatty acids in RBC membrane.

†Omega-3 index: content of EPA + DHA in RBC membrane. Apo B, apolipoprotein B; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LDL-P, low-density lipoprotein particles; non-HDL-C, non-high-density lipoprotein cholesterol; RBC, red blood cell; TC, total cholesterol; TGs, triglycerides. Conclusions: Combining a highly purified prescription EPA (icosapent ethyl) with 10% loss of body weight in a high-risk obese patient with diabetes and statin intolerance led to improvements in HOMA-IR and atherogenic dyslipidemia with substantial beneficial changes in insulin, A₁C, glucose, TGs, TC, LDL-C, non-HDL-C, Apo B, and

LDL-P, along with improvements in the TG/HDL-C ratio and omega-3 index, over a 3-month period.

PATIENT CHARACTERISTICS AND REAL WORLD EFFECTIVENESS OF DAPAGLIFLOZIN: AN OBSERVATIONAL ANALYSIS OF US ELECTRONIC HEALTH RECORDS

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Background: Dapagliflozin, a sodium-glucose cotransporter-2 inhibitor FDA-approved in 2014, lowers blood glucose in adults with type 2 diabetes (T2D) by reducing renal glucose reabsorption.

Objective: To examine characteristics of patients initiating dapagliflozin in routine clinical care and assess its effect on A1C and body weight.

Methods: This retrospective, observational study used an electronic health record database including data from primary care and specialty practices. The study cohort included patients with T2D first prescribed dapagliflozin between January 2014-March 2015, who had ≥ 6 months of data before that prescription and who remained in the database for ≥ 3 months after dapagliflozin initiation. Patient characteristics, changes in A1C, weight, and eGFR were analyzed.

Results: Of 9565 patients with ≥ 1 prescription for dapagliflozin, 6450 met inclusion criteria. Mean (SD) age was 51.7 (10.1) years, and 51.9% were men. Mean (SD) baseline characteristics were: weight, 105.1 (25.0) kg; BMI, 36.0 (7.6) kg/m²; A1C, 8.64% (1.7%); eGFR, 100.6 (17.6) mL/min/1.73m². At ≥ 6 months, in key subgroups (n = 4286) of patients using add-on dapagliflozin to metformin (14.4%), in regimens with ≥ 3 therapies (43.6%), or with insulin (8.5%), the proportion of patients with A1C <8% increased from 39% to 60%, and the proportion with A1C >9% decreased from 35% to 21%. Mean (SD) change in weight was -2.4 (6.5) kg, and eGFR remained stable (mean [SD] change: -3.37 [14.33] mL/min/1.73m²).

Conclusion: Reductions in A1C and weight, and stable eGFR observed in the real-world setting were consistent with results from the dapagliflozin clinical trial program.

1-HOUR ELEVATED PLASMA GLUCOSE LEVELS ARE ASSOCIATED WITH METABOLIC SYNDROME IN PATIENTS WITH IMPAIRED FASTING GLUCOSE

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Objective: To evaluate the association between 1-hour elevated plasma glucose levels and Metabolic Syndrome in patient with impaired fasting glucose (IFG).

Methods: In an analytic transversal study, we evaluated 258 patients with IFG at the Endocrinology Department of the Air Force Central Hospital (AFCH) in Lima-Perú from July of 2013 to June of 2015. Patients with diagnostic of type 2 diabetes (T2DM), thyroid or cardiovascular disease, treatment with antipsychotic drugs or corticosteroids and pregnant were excluded. All patients were evaluated with a 75 gr Oral Glucose Tolerance test (OGTT) with sampling at baseline and at 60 and 120 min. We measured lipid profile, liver enzymes (aspartate transaminase or AST and alanine transaminase or ALT), uric acid and obtained anthropometrics measurements such as body mass index and abdominal circumferences. Metabolic Syndrome (MS) was define according to the "Harmonizing the Metabolic Syndrome".

Results: We found 30 subjects with newly diagnosed T2DM and 54 subjects with impaired glucose tolerance (IGT). The number of patients with normal glucose tolerance (NGT) was 174. Among patients with NGT, 40% had 1-hour OGTT glucose > 155 mg/dL (1hOGT). In the group of NGT, patients with 1hOGT had a significant association with MS (OR = 1.95). Although we found a less association between IGT and MS (OR = 1.36) in the study population. We additionally found a positive association between 1hOGT with BMI, AST and uric acid in subjects with NGT (OR = 1.68, 1.05 and 1.79, respectively).

Conclusion: We found a strong association between 1-hour OGTT glucose of >155 mg/dL and MS in patients with NGT. 1hOGT could be a good predictor of MS, consequently cardiovascular risk, in subjects with an elevated fasting glucose.

PREVIOUS METABOLIC AND INSULIN RESISTANCE PROFILE OF A COHORT OF YOUNG HISPANIC MEN WITH NAFLD WHO PROGRESS TO PREDIABETES

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Aim: To evaluate the insulin resistance level, fasting and the 2-hour plasma glucose levels in a normoglycemic cohort of Colombian Army diagnosed with NAFLD who progressed to prediabetes.

Methods: Review of Medical Records of 70 patients from 2008 until 2015, previously characterized as normoglycemic and with NAFLD. International criteria for diagnosis

of prediabetes/diabetes were used. The data was analyzed with the statistical program SPSS.

Results: Enough information was obtained from 55 clinical records. Actually patients have an average age of 46 ys. No one progressed to diabetes, 34.5% (n = 19) progressed to prediabetes. The analysis from the previous metabolic profile was done with the T-student test, comparing the normoglycemic group vs prediabetic group. Statistically significant differences were found only for fasting plasma glucose (x: 95.8 vs 88.8 p: 0.01) and the 2-Hour plasma glucose (x: 102.6 vs 83.4 p: 0.004) GGT (x: 97 vs 59.2 p: 0.02). The mean HOMA index was 2.45 in prediabetics patients vs 2.30 in normoglycemic patients. This difference wasn't statistically significant (p: 0.662)

Conclusions: Our results remark the need for a deeper screening in patients with some pathological entities as NAFLD and maybe, the need of reevaluate the glycemia and HOMA cut points, at least for Hispanic population.