Session 1

Asian Session 1(Complication)

Chair: Daisuke Yabe (Kansai Erectric Power Hospital, Japan)

May 22, 2009 (Fri)13:10-14:10

Poster Presentation Room (Osaka International Convention Center, 10F, Conference Room 1004-7)

II-P-30 Chronic Complications in Type 2 Diabetic Patients Followed at Kossamak Hospital, Phnom Penh, Cambodia in 2008

Seng S., et al.
Kossamak Hospital, Phnom Penh, Cambodia

Background: Previous surveys indicated high prevalence of diabetes in Cambodia.
Objective: To study complications and metabolic syndrome (MS) in type 2 Diabetic Patients (T2DP) in Phnom Penh.
Design and Results: 101 T2DP (median age: 55y; range: 35-80) were followed at Kossomak Hospital (70 female, 31 male). In the female T2DP, 84% had waist circumference (WC) ≧ 80 cm; in the male 64% ≧ 90 cm. 54% of the female, 58% of the male were considered hypertensive (with either systolic BP ≧ 130 mm Hg or diastolic BP ≧ 85 or antihypertensive treatment). In the female, 66% had plasma TG ≧ 150 mg/dl, 66% HDL cholesterol < 50 mg/dl; in the male, 71.0 % TG ≧ 150, 51.6% HDL cholesterol < 40. According to 2005 IDF criteria, 80% of the female had MS versus 58% of the male. Among all T2DP, retinopathy was present in 17, neuropathy (N) in 36 (without gender difference). HbA_{1c} was between 6.1 and 7% in 14 patients; 7.1 and 8% in 29; 8.1 and 10% in 25; 10.1 and 12% in 14; >12.1% in 16. Reported diabetes duration varied between 1 and 16 y. Patients with N had mean diabetes duration of 8.3 y; those without N, 3.3y. Patients with N had a median HbA_{1c} of 9.6%, those without N 8.7%.
Conclusion: High MS or neuropathy frequencies and HbA_{1c} levels were the striking findings.

II-P-31 Management of Diabetic Foot: Endovascular Recanalization of Critical Limb Ischemia

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Introduction: Diabetic Foot is the main reason for limb loss. We evaluated the outcomes of limb-salvage angioplasty in diabetic patients with Critical Limb Ischemia (CLI). Methods: We analysed retrospectively results of 29 consecutive high surgical risk patients with CLI treated with PTA/Stent. All patients had occlusion of previous bypass graft. Pre- and post-procedural ankle-brachial index, TcPO2 and TcPCO2 were measured. Ulcers were photographically recorded for core laboratory assessment. Follow-up was scheduled 1, 3, 6 months and yearly thereafter. Results: The technical success was achieved in 28 (93.3%) of 30 limbs. Pre-procedural level of TcPO2 was 13.8 ± 6 mmHg; in patients with technical success this parameter was increased up to 52.4 ± 0.22 ($p<0.001$). Preprocedural mean of TcPCO2 was 71.2 ± 27 mmHg, but postprocedural mean, after first week, was decresed significantly. ($p<0.001$) The ABI improved to 0.86 ± 0.18 ($p<0.001$ versus pretreatment).The mean area reduction of ulcers or minor amputation sites was 93% at 6 months. Conclusion: Limb-salvage angioplasty can be successfully achieved in diabetic patients with CLI with optimal results.

II-P-32 Characteristics and Treatment Results of Foot Ulcer in Diabetic In-patients in Hospital of Endocrinology of Vietnam

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Background: Diabetic foot ulcer is one of the most severe complications with very poor outcome particularly in developing countries like Vietnam.
Objectives: The present study aims at describing characteristics of foot ulcers and their treatment results in diabetic in-patients.
Methods: Two hundred and fifty diabetic patients with foot ulcer hospitalized in the National Hospital of Endocrinology of Vietnam for 2007 and 2008 were included in the study. Clinical and laboratory characteristics were assessed and the treatment results evaluated.
Results : The mean age was 60.9 years, the women made up 62.7%, the mean diabetes duration 6.97 ± 5.75 years, the mean fasting plasma glucose level was 14.7 ± 7.4 mmol/l and that of HbA_{1c} 9.7 ± 2.8%. Infectious ulcer, lost of foot sensation, peripheral arterial disease, foot deformity and past foot ulcer or amputation was present in 91.3%, 84.4%, 44.8%, 35.2% and 44.6%, respectively. The ulcers of grade 2 and 3 by Wagner's classification made up 28.8%. The amputation rate was 24.4%. The mean hospital stay was 24.3 days.
Conclusions: Diabetic patients with foot ulcer had poor blood glucose control, high rate of infection leading to high rate of amputation.

II-P-33 Diabetic Retinopathy in Ulaanbaatar, Mongolia

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Health Sciences University of Mongolia, Mongolia

Aim: To establish the prevalence, severity, and risk factors for diabetic retinopathy in randomly selected type 2 diabetic patients in Ulaanbaatar city.
Methods: Two hundred forty six patients from 6 districts in Ulaanbaatar were included in this study. Participants provided a detailed medical and personal history and underwent an ocular examination including funduscopy and provided blood sample, from which the blood glucose was measured.
Results: The prevalence of diabetic retinopathy among people with type 2 diabetes was 29.2%. The prevalence of untreated, vision-threatening retinopathy was 2.4%. Retinopathy was positively associated with a longer reported duration of diabetes and with higher fractions of blood glucose ($p<0.01$). Loss of visual acuity correlated with progression of retinopathy (p-0.003).
Conclusion: Diabetic retinopathy is common risk for loss vision among type 2 diabetic patients in Mongolia.The strict glycaemic control and regular follow up would prevent from diabetic retinopathy.

II-P-34 Retinopathy Characteristics in Type 2 Diabetic Patients Followed at Kossamak Hospital, Phnom Penh, Cambodia in 2008

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Department of Ophthalmology, Preah Ang Duong Hospital, Phnom Penh, Cambodia

Background: Previous surveys indicated high prevalence of diabetes in Cambodia.
Objective: To report the characteristics of diabetic retinopathy occurring in Type 2 Diabetic Patients (T2DP) in Phnom Penh.
Design and Results: 101 T2DP (median age: 55y; range: 35-80) were followed at Kossomak Hospital (70 female, 31 male). Their other characteristics are reported in the abstract presented here by Seng et al.
Results: Among all T2DP, retinopathy was present in 17 (17% of the female, 16% of the male); 15 presented moderate nonproliferative diabetic retinopathy (score 2) ; 2, severe nonproliferative diabetic retinopathy (score 3). 2 had also Diabetic Macular Edema. Other ocular findings were observed: Cataract, Glaucoma, Refractive Errors, Pterygium Corneal Scar, Optic Atrophy, Retinitis Pigmentosa.
T2DP with retinopathy had mean reported diabetes duration of 7.4 y; those without retinopathy, 4.6 y. T2DP with score 3 retinopathy had a median HbA_{1c} of 10.5%; those with score 2 9.3%, those without retinopathy 9.0%.
Conclusion: Retinopathy was found in 17% of T2DP whose HbA_{1c} levels were particularly elevated in general.

II-P-35 Prevalence and Risk Factors of Diabetic Neuropathy in Mongolia

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Background: The aims of this study were to evaluate the diabetic neuropathy and risk factors of diabetic neuropathy among type 2 diabetic patients in Mongolia.
Methods: This study included 285 type 2 diabetic patients, with a mean age of 58.81 ± 11.03 years and a mean diabetes duration of 5.06 ± 5.68 years.
Results: DPN and CAN were 178(68.0%) and 107(52.8%). Symptoms of sudomotor, genitourinary, gastrointestinal autonomic neuropathy and impotentia in male were 87.3%, 72.5%, 43.7% and 74.2%. People with no clinical (Stages 0/1), clinical (Stage 2) and late complications of clinical (Stage 3) of DPN were 84(32.1%), 138(52.7%) and 40(15.3%). Risk factors for development and progression of neuropathy such as poor glycemic control, hypertention and hyperlipidemia were 239(88.5%), 139(48.8%) and 129(52.7%). Diabetic neuropathy related with diabetes duration and age ($p<0.01$).
Conclusions: The DPN and CAN in Mongolian type 2 diabetic patients were 68.0% and 52.8%. One of most important risk factors for development and progression of diabetic neuropathy was poor glycemic control.

II-P-36 The Influence of Homocysteine, Homocysteine Thiolactone on Diabetic Vasculopathy

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Objective: To study the role of homocysteine thiolactone (HcyT) and homocysteine(Hcy) in the development of macro/micro-anginopathy in Chinese patients with type 2 diabetes. Methods: A total 160 subjects were recruited in this study. Plasma Hcy, HcyT, folic acid and Vitamin B12 levels were measured. Results: Plasma Hcy and HcyT concentrations in diabetic patients were significantly higher than that in healthy controls. Plasma Hcy and HcyT levels in patients with macroanginopathy tended to be higher. With the progression of diabetic retinopathy and nephropathy, the Hcy and HcyT concentrations were increased gradually. HcyT, Hcy were associated with the risk of diabetic macroanginopathy significantly. Conclusions: Hcy and HcyT were involved in the development and progression of diabetic macro/micro vasculopathy. HcyT might provide a plausible chemical mechanism in explaining Hcy toxicity to the human vascular endothelium.

II-P-37 Lack of Distinct Glycemic Thresholds in Identifying Microvascular Complications. The Singapore Prospective Study Program

Chin Meng Khoo, Nang Ei Ei Khaing, E Shyong Tai, Su Chi Lim, Subramaniam Tavintharan, Tien Yin Wong, Derrick Heng, Jeannette Lee
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Recent studies suggest that no distinct glycemic threshold consistently differentiates individuals with or without retinopathy. Whether the same was true for other microvascular complications is not known. We studied 5,094 participants with FPG and microvascular assessment from four previous cross sectional surveys carried out in Singapore (1982 to 1998) who completed a follow-up examination (2004 to 2007). Peripheral neuropathy (PN) was diagnosed based on abnormal responses to 10 g monofilament or neurothesiometer, albuminuria if urine albumin-to-creatinine ratio >30 ug/mg and chronic kidney disease (CKD) if eGFR <60 mL/min/1.73m2. The prevalence of PN was 5.0%, albuminuria 12.6% and CKD 6.2%. Although each outcome was more prevalent in participants defined to have diabetes mellitus (DM), the prevalence of these outcomes increased gradually in relation to FPG, beginning at levels of FPG below the existing diagnostic threshold for DM of 7 mmol/L. Current diagnostic thresholds for DM have limited sensitivity for identifying individuals with these microvascular complications. Other means of identifying these individuals may benefit the public health.

II-P-38 Effect of Dipeptidyl Peptidase-IV (DPP-IV) Inhibitor (Vildagliptin) on Peripheral Nerves in Streptozotocin-induced Diabetic Rats

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The aim of this study is to investigate the GLP-1 pathway effect on the peripheral nerves using a DPP-IV inhibitor in streptozotocin (STZ) induced diabetic rats. The adult male Sprague-Dawley (SD) rats were divided into four groups, two groups (n=6 in each) were given a DPP-IV inhibitor of 0.3mg/kg/day and 10mg/kg/day respectively, dissolved in water. The other groups (diabetic without any treatment and normal glucose group) were given the same volume of water (n=6 in each). At 0, 16, and 32 weeks, intraepidermal innervation from dorsal skin was quantified as nerve fiber abundance per unit length of epidermis (IENF/mm). The results are as follows (IENF/mm): Normal (9.89 ± 0.34), DM (8.42 ± 0.28), DM with 0.3mg/kg DPP-IV inhibitor (9.88 ± 0.38), and DM with 10mg/kg DPP-IV inhibitor (10.36 ± 0.32) ($P < 0.05$). And the reduction of IENF density are as follows (% changes): Normal (10.1%), DM (25.8%), DM with 0.3mg/kg DPP-IV inhibitor (13.3%), and DM with 10mg/kg DPP-IV inhibitor (7.9%) ($P < 0.05$). Our study indicated that a DPP-IV inhibitor can prevent from peripheral nerve degeneration and support the idea that GLP-1 may be useful in peripheral neuropathy.

Session 2

Asian Session 2(Diagnosis/Pathophysiology/Epidemiology)

Chair: Nam Han Cho (Department of Preventive Medicine, Ajou University School of Medicine, Korea)

May 22, 2009 (Fri) 13:10-14:10

Poster Presentation Room (Osaka International Convention Center, 10F, Conference Room 1004-7)

II-P-39 Progressive Loss of β-Cell Function is the Major Contributor to Increasing Fasting Glucose in Chinese

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Aims: To evaluate the relative role of insulin resistance and β-cell function to worsening glucose tolerance and increasing fasting plasma glucose (FPG) in Chinese subjects.
Methods: 982 Chinese subjects between 18 and 80 years of age underwent an oral glucose tolerance test (OGTT). Categories of glucose tolerance were defined according to 1999 World Health Organization criteria. We also separately subdivided the normal glucose tolerance (NGT) group into 4 groups according FPG levels: NGT1: FPG $<$ 4.5 mmol/l, NGT2: 4.5 $\leqq$ FPG $<$ 5.0 mmol/l, NGT3: 5.0 $\leqq$ FPG $<$ 5.6 mmol/l, NGT4: 5.6 $\leqq$ FPG $<$6.1 mmol/l.
Results: Decreasing glucose tolerance was associated with increasing insulin resistance and decreasing β-cell function. Increasing fasting blood glucose was also associated with decreasing β-cell function, whereas the insulin resistance indicated by HOMA-IR were comparable among NGT groups.
Conclusions: Our study showed that both impaired β-cell function and insulin resistance are associated with impaired glucose metabolism, and that β-cell function may be more important in determining glucose disposal among Chinese subjects.

II-P-40 Optimal Fasting Plasma Glucose for Diagnosis of Diabetes in a Singapore Population is Lower Than The WHO Recommendation

Joan Khoo, Richard Chen, Vanessa Au, Edward Pratt
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Aim: Diabetes mellitus (DM) is defined by the World Health Organization (WHO) as fasting plasma glucose (FPG)$\geq$ 7.0 mmol/liter (mM,) or 2-hour post-load glucose (2HPG)$\geq$11.1 mM in a 75-gram oral glucose tolerance test (OGTT). We aim to find the optimal FPG that corresponds with 2HPG 11.1 mM in a Singaporean population.
Methods: 787 subjects underwent 75-g OGTT in the outpatient clinics of a Singapore hospital from 2001-2007. Regression models and receiver operating characteristic (ROC) curves were used to define optimal FPG.
Results: Mean age of our patients was 50.0 $\pm$ 15.4 years (range 14-93). Average FPG was 6.5 $\pm$ 2.8 mM (3.0-24.5), and mean 2HPG was 11.0 $\pm$ 5.6 mM (3.2-36.4). Exponential regression model was the best fit (highest R2). FPG corresponding to 2HPG 11.1 mM was 6.1 mM. FPG by ROC analysis was 6.0 mM (sensitivity 81.5%, specificity 82.0%, area under curve 0.90).
Conclusion: The FPG for diagnosis of diabetes in our population is lower than WHO criteria.

II-P-41 Prevalence of Diabetes Mellitus in Jakarta

Dante Saksono Harbuwono, Dyah Purnamasari, Sidartawan Soegondo, Tri Juli Edi, Yunir Budiman Em, Suharko Soebardi, Gatut Semiardji, Maryantoro Oemardi, Pradana Soewono, Sarwono Waspadji, Boedi Santoso, Imam Subekti
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In 1982 and 1992, the prevalence of DM in two regions of Jakarta (North Jakarta and East Jakarta) were 1.7% and 5.7% respectively. In 2001, the prevalence of DM in Depok, a suburban area near to Jakarta, was 14.7%. Jakarta, the capital city of Indonesia, is divided into five townships (north, south, east, west and central) with 8.4 million inhabitants and similar proportion between men and women. From the 1800 subjects who were selected, 1645 subjects completed this study (91.4% respons rate). The prevalence of diagnosed DM, undiagnosed DM and (total) DM were 3.7%, 7.7% and 11.4% respectively. After adjusted to age and sex, the prevalence of DM in Jakarta is 8%. **Diagnosed diabetes** The crude prevalence of diagnosed DM in this study is 3.7% and many of them were in the range of 50-59 years. **Undiagnosed DM** The crude prevalence of undiagnosed DM is 7.7% and many of them are in the range of 60-64 years. Prevalence of undiagnosed DM in women was about twofold increased at the age of 40-49 and 50-59 and still increasing thereafter. While the prevalence of undiagnosed DM in men increased about twice in the age of 40-49 and remain flat thereafter. After adjusted to age and sex, the prevalence of undiagnosed DM in men and women are 2% and 6% respectively.

II-P-42 U-Shape Relationship between Both Fasting and Postprandial Glucose Levels and Mortality for Type 2 Diabetes

Yi-Der Jiang, Hung-Yuan Li, Tien-Jyun Chang, Lee-Ming Chuang
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Aim: To evaluate the role of fasting (FPG) and postprandial glucose (PPG) levels on all-cause and cardiovascular mortalities. Methods: A diabetes cohort was established since Jul 1996 at National Taiwan University Hospital. Till Dec 2003, 1744 males and 1695 females over 40 years old type 2 diabetic patients were recruited. Their mean age was 61.0 ± 10.3 and HbA_{1c} 7.61 ± 1.43 %. Survival status was followed till Dec 2007, with a mean follow-up of 7.16 ± 2.43 years. Results: There is a U-shape for mortalities and FPG. Statistical significant increases of mortality were observed when a mean FPG level below 100 or over 140 mg/dl. The relation between PPG and mortality showed a similar U-shape curve. Statistical significant increases of mortality were observed when a mean PPG level below 140 or over 200 mg/dl. Conclusions: Due to the U-shape for glycemia and mortalities, over-treatment should be cautious, while FPG over 140 mg/dl or PPG over 200 mg/dl should be aggressively controlled.

II-P-43 Correlation of Abdominal Obesity and Lipid Profile in Type 2 Diabetes Outpatient in Sanglah Hospital, Bali-Indonesia

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Endocrinology and Metabolism Division, Department of Internal Medicine, Faculty of Medicine Udayana University/ Sanglah Hospital Denpasar Bali, Indonesia

Objective: To determine the correlation between abdominal obesity with lipid profile in type 2 diabetes
Methods: A cross sectional study was conducted at outpatient clinic Sanglah Hospital in January-February 2008.
Results: There were 355 type 2 diabetes, male:female 58.6%:41.4%, age 55.8 ± 8.9 (24-77) years. BMI was 25.1 ± 4.2 kg/m2. In general 48.6% were obese, however based on the waist circumference (WC), abdominal obesity were 62.3%. WC was correlated significantly with lipid profile including total cholesterol (r0.131, $p<0.05$), HDL(r-0.160, $p<0.01$), TG (r0.175, $p<0.01$), ratio total cholesterol/HDL (r0.230, $p<0.01$). Among group with and without abdominal obesity we found differences in total cholesterol 204.4 ± 42.2 vs 189.7 ± 58.3 (p0.019), TG 128.8 ± 75.6 vs 102.1 ± 63.4 (p0.005), and ratio of total cholesterol/HDL 4.9 ± 1.3 vs 4.4 ± 1.5 (p0.013).
Conclusion: Lipid profile in type 2 diabetes with and without abdominal obesity has a significance differences, and WC may act as a simple predictor for lipid disorders in type 2 diabetes and should regularly measured.

II-P-44 Prevalence of Metabolic Syndrome among Mongolians

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Background and aims: Metabolic syndrome is one of high risk in Mongolian population.
Materials and methods: We examined 3411 Mongolians for Metabolic syndrome based on the modified definitions of the working definition proposed by the IDF in 2006.
Results: The prevalence of metabolic syndrome was 20.1 percent. Alcohol consumption and smoking were 67% and 32.5 among population with metabolic syndrome. The prevalence of hypertriglyceridemia (2.26 mmol/l and above) among the subjects with metabolic syndrome was 53% (+0.05) presenting higher prevalence in males by 4.2% as compared to females. The 92.7 (+0.1) percent of subjects with metabolic syndrome had elevated blood pressure, and 85.4 percent of subjects with metabolic syndrome were low active life style ($p<0.01$). It is low significant to alcohol consumption either smoking ($p<0.05$, $r=0.315$). But it was high significant to lack of physical activity vs. developing metabolic syndrome ($p<0.01$, $r=0.885$).
Conclusion: The prevalence of metabolic syndrome in Mongolia is 20.1 percent. The lack of physical activity causes developing metabolic syndrome significantly.

II-P-45 Association Between Serum Uric Acid Concentration and Insulin Resistance on Balinese People in Tenganan Region

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The reduction of endothelial nitric oxide bioavailability and the production of reactive oxygen species by uric acid may be a mechanism for insulin resistance. To know the association between serum uric acid concentration and insulin resistance, a cross sectional analytic study was conducted on Balinese in Tenganan region. Of 80 eligible samples, mean of serum uric acid concentration was 5.49 ± 1.38 mg/dl, median of HOMA-IR was 0.685 (0.38-4.10). There was association among serum uric acid with insulin resistance (r=0.231; *P*=0.039) respectively. But association between serum uric acid and insulin resistance not confirmed by multiple logistic regression, (PR 0.675; CI 95%: 0.167-2.725; *P*=0.581).Waist circumference has independent association with insulin resistance with PR 6.958; CI 95%: 1.596-30.341; *P*=0.010. Conclusion: Serum uric acid is associated with insulin resistance, but serum uric acid is not independent predictor for insulin resistance.

II-P-46 The Diagnostic Value of Protein Tyrosine Phosphates Antibody for Latent Autoimmune Diabetes in Adults

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Objective: To explore the diagnostic value of protein tyrosine phosphates antibody (IA-2A, IA-2 antibody) on Latent Autoimmune Diabetes in Adults (LADA, Slowly progressive type 1 diabetes). Methods: Radioligand assay was used to test IA-2A and glutamic acid decarboxylase antibody (GAD-Ab) in 2,027 patients with newly diagnosed type 2 diabetes mellitus (T2DM). Results: The positive rate of IA-2A was 2.2%, lower than GAD-Ab (2.2% vs 10.6%, $P<0.001$), united measurement increased the rate by 1.1%. The detection rate of IA-2A was higher in the low birth weight, low C-peptide group ($P<0.05$). Compared with T2DM, single IA-2A positive patients were more dependent on insulin therapy ($P<0.05$). The characteristics of high-titer IA-2A positive patients were as the followings: smaller onset age, shorter course ($P<0.01$); lower body mass index, lower fasting C-peptide and higher predisposition of insulin therapy ($P<0.05$). Conclusion: GAD-Ab and IA-2A jointly detection can improve the sensitivity for diagnosing LADA. The IA-2A positive LADA patients were inclined to insulin therapy, while the characteristics of high titer ones were close with type 1 diabetes.

II-P-47 Prevalence, Clinical and Immunologic Features of Fulminant Type 1 Diabetes Among Chinese Hunan Han Population

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Objective: To investigate the prevalence, clinical and immunologic features of fulminant type 1 diabetes (F1D) among Chinese Hunan Han population. Research Design and Methods: F1D were screened from impatients with diabetes of the second Xiangya Hospital from 2001 to 2008. Clinical data were obtained by reviewing medical records. GAD-Ab, IA2-Ab and ZnT8-Ab were tested by radioligand assay. Results: Among consecutive 9493 hospitalized cases of diabetes, eleven F1D were screened. Another 13 F1D outside our hospitals were also enrolled. Three F1D associated with preganancy and another three F1D associated with drug-induced hypersensitivity syndrome were identified. Interestingly, 8 out of 20 F1D patients were at least one islet autoantibody positive on admission. Conclusions: F1D accounts for 0.1% of hospitalized patients with diabetes in Chinese Hunan Han population. Autoimmunity may be involved in the pathogenesis of part of F1D.

Session 3

Asian Session 3(Genetics/Cellular Biology)

Chair: Yukio Horikawa (Gifu University Hospital, Japan)

May 22, 2009 (Fri)13:10-14:10

Poster Presentation Room (Osaka International Convention Center, 10F, Conference Room 1004-7)

II-P-48 The Protective Effects and Potential Mechanisms of TZDs on Pancreatic β-Cell Line NIT-1

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Diabetes Center, Metabolic Syndrome Research Center, Institute of Metabolism and Endocrinology, Central South University, China

Objective: To investigate the protective effects and potential mechanisms of TZDs on pancreatic β-cells. Methods: The apoptosis of NIT-1 cells were induced by treatment with interleukin-1β(IL-1β) and interferon-γ(IFN-γ) in vitro. The NIT-1 cells were treated with rosiglitazone (RSG) /pioglitazone (PIG) at different levels. The apoptosis rate and Caspase-3 specific activity of NIT-1 cells were determined by Hoechest33342 staining, Caspase-3 Assay, Annexin V-FITC/PI flow cytometry, respectively. Insulin secretion of NIT-1 cells was measured by ELISA. Results: After treatment of different concentrations of RSG/PIG, the apoptosis rate and caspase-3 activity of NIT-1 cells decreased at different levels. There were significant differences in apoptosis rate and caspase-3 activity between the RSG/PIG treatment group and IL-1β/IFN-γ group ($P<0.01$), the most protective effect was seen with the concentration of 10uM. IL-1β/ IFN-γ apparently inhibited glucose-stimulated insulin secretion (GSIS) of NIT-1 cells without any treatment ($P<0.01$). After treatment with RSG/PIG, GSIS of NIT-1 cells recovered in different degrees ($P<0.01$), the RSG treatment group was more effective compared with PIG treatment group ($P<0.05$). Moreover, most of the protective effects of TZDs on pancreatic β-cells can be blocked by PPAR-γ inhibitor GW9662. Conclusion: TZDs are shown to protect β-cells function via inhibiting cytokine-induced apoptosis, which may be correlated with down-regulation of caspase-3 activity.

II-P-49 Functional Analysis of R325W Variant in the Zinc Transporter-8 Gene (*SLC 30A8*) in Pancreatic β Cell

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Objective: Recent genome association studies have revealed that the islet specific zinc transporter-8 polymorphism (R325W *SLC30A8*, rs13266634) is associated with type 2 diabetes (T2DM). However the underlying molecular mechanism was unknown. Here we investigated the functional aspect of this polymorphism in pancreatic beta cell.
Methods: We made mutant type *SLC30A8* cDNA by site-directed mutagenesis. Wild-type and mutant-type *SLC30A8* constructs were transfected into INS-1E cells. We analyzed the amount of insulin secretion in response to glucose loading and sulfonylurea treatment.
Results: There was no difference in amount of insulin secretion between wild-type and mutant when no glucose was loaded. INS-1E cells transfected with mutant cDNA produced more insulin than cells transfected with wild-type *SLC30A8*. This difference was augmented by adding sulfonylurea.
Conclusions: These data provide the functional evidence that the *SLC30A8* rs13266634 genetic variation affects insulin secretion and thereby associating its genetic variation with T2DM.

II-P-50 PAX6 Regulates Glucose Metabolism via Proinsulin Processing Mediated by Prohormone Convertase 1/3

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Heterozygous *PAX6* mutations can lead to glucose intolerance in human. Conditional inactivation of *Pax6* in pancreas of mice causes diabetes, but the underlying molecular mechanism is largely unknown. Here we provided evidence that patients with *PAX6* R240Stop mutation in an aniridia pedigree also had abnormal glucose metabolism. The underlying mechanism was further investigated using *Pax6* R266Stop mutant small-eye mice, which also have abnormal glucose metabolism similar to that in *PAX6* R240Stop mutation human aniridia patients. Heterozygous *PAX6* deficiency, both in aniridia patients with a *PAX6* R240Stop mutation and in mice with *Pax6* R266Stop mutation, causes defective proinsulin processing and abnormal glucose metabolism. *PAX6* can bind to the promoter and directly up-regulate production of prohormone convertase (PC)1/3, an enzyme essential for conversion of proinsulin to insulin. *Pax6* mutations lead to PC1/3 deficiency, resulting in defective proinsulin processing and abnormal glucose metabolism. Our study elucidates a novel mechanism by which PAX6 regulates glucose metabolism via PC1/3-mediated insulin processing.

II-P-51 withdrawn

II-P-52 Heritability of Insulin Sensitivity in Adolescent Twin/Sibling: OGTT-Based *Versus* Fasting-Based Indices

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Insulin resistance plays a crucial role in many metabolic abnormalities and metabolic syndrome. We aim to evaluate the importance of genetic and environmental effects on insulin sensitivity indices derived from fasting state and during oral glucose tolerance test (OGTT) in a sample of adolescent twin/siblings. We recruited a total of 228 twin/sibling pairs aged 12 to 18 from the middle schools for a 2h OGTT. Univariate analyses using structural equation modeling implemented in Mx software were employed. A moderate to high broad heritability (27%-78%) was estimated for all insulin sensitivity indices except for GSI. Also, no significant sex differences were found. The additive genetic contribution to the variation in fasting-based indices explained by ADE model was around 25%, whereas the estimates of broad heritability were around 55%. Furthermore, genetic effects appeared to be 63%-78% for OGTT-based insulin sensitivity indices better explained by ADE model. In addition, significant additive genetic influences were observed for OGTT-based indices better explained by ACE model. Among them, the broad heritability of SIisOGTT index was as high as 75%. These findings revealed that the broad heritability estimates were greater for OGTT-based than fasting-based indices. The findings may help in the search for genes underlying the variation in complex traits that are affected by insulin sensitivity.

II-P-53 Association of GWAS Identified Type 2 Diabetes Susceptibility Loci in the Chinese, Malay and Asian-Indians in Singapore

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Objective: Novel type 2 diabetes (T2D) susceptibility genes, identified through GWAS, have been replicated in many European and Japanese populations. However, these loci are less well characterized in other Asian populations. The aim of this study was to examine the effects of SNPs at 8 T2D susceptibility loci in Chinese, Malays and Asian-Indians in Singapore.
Methods: We genotyped the candidate SNPs in 9036 subjects from three cross-sectional studies in Singapore. We also performed a meta-analysis of our results with nine published studies in Asia.
Results: Combined analysis of the ethnic groups revealed associations between *CDKAL1* (OR=1.13, $p=1x10^{-5}$), *CDKN2A/B* (OR=1.16, $p=3x10^{-5}$), *HHEX* (OR=1.14, $p=2x10^{-4}$), *SLC30A8* (OR=1.06, p=0.039) and *KCNQ1* (OR=1.20, $p=1x10^{-7}$) with T2D.
Conclusions: Diabetes susceptibility loci identified through GWAS are relevant in Asian populations. We have shown for the first time that *CDKN2A/B, HHEX, SLC30A8* and *KCNQ1* confer an increased risk of T2D in Malays.

II-P-54 A Genetic Variation in Human SORBS1 Gene is Associated with Blood Pressure Regulation: A Family-Based Association Study

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The pathogenesis of essential hypertension is unknown although it is frequently associated with insulin resistance and metabolic syndrome. Previously we have identified a genetic polymorphism of T228A in the human SORBS1 gene which has been shown to associate with insulin resistance, obesity and type 2 diabetes in human. Here we performed a family-based association study using 602 families of Chinese and Japanese descents collected in a previous study of SAPPHIRe for searching for genetic factors of hypertension. We found that 228A-allele was significantly associated with a lower level of diastolic blood pressure and mean arterial pressure in a recessive mode of action. The siblings with AA genotype of the SORBS1 gene carried a reduced risk to hypertension (adjusted OR=0.18, 95% CI: 0.0460~0.7024, p=0.0136) after adjustment for age, gender, BMI and ethnicity. The protective role of AA genotype of the SORBS1 gene for blood pressure regulation and hypertension status was independent of various confounding factors by multiple regression analyses. In a subset of 220 pedigrees with information of marker data from affected, unaffected siblings and satisfying the minimal structure for sibling-based transmission-disequilibrium test, we found a significant linkage between T228A polymorphism of the SORBS1 gene and hypertension (Z score= 3.178, p=0.000742). These results strongly provide evidence for a novel susceptibility gene on chromosome 10q for essential hypertension.

II-P-55 Central Administration of Endoplasmic Reticulum Stress Inducers Inhibits the Anorexigenic Effects of Leptin and Insulin

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Leptin and insulin are important anorexigenic hormones acting on the hypothalamus. However, most obese humans and animals have reduced hypothalamic response to leptin and insulin. Increased endoplasmic reticulum (ER) stress has been shown to cause insulin resistance in the livers of obese animals. We therefore assessed the role for ER stress in obesity-associated hypothalamic leptin and insulin resistance in diet-induced obesity (DIO) animal models. We found that the expression levels of ER stress markers, glucose-regulating protein-78 (GRP78) and C/EBP homology protein (CHOP) were increased in medio-basal hypothalamus of high-fat-diet (HFD)-fed obese mice compared to low-fat-diet (LFD)-fed mice. Expression of phosphorylated c-Jun, a marker of JNK activation, was also increased in the hypothalamus of DIO mice. Intracerebroventricular (i3V) administration of thapsigargin, ER stress inducer, increased food intake and body weight. Furthermore, i3V or intra-hypothalamic administration of thapsigargin inhibited the anorexigenic and weight-reducing effects of leptin and insulin. Therefore, increased hypothalamic ER stress in obese animals may cause central leptin and insulin resistance.