

QTcI prolongation ($p < 0.001$ in all three groups). Abnormal QTcI (> 440 msec) was seen significantly more often in patients with CAN compared to those without CAN ($p < 0.001$ in nonalcoholic diabetics and nondiabetic alcoholics, $p < 0.05$ in alcoholic NIDDM subjects). Analysing the connection between QTcI and the five reflex tests separately, significant negative correlations indicate that beside the previously established role of sympathetic imbalance even parasympathetic damage contributes to the development of QTcI-lengthening.

Conclusions: Our data provide evidence of a relationship between the presence and severity of cardiovascular autonomic neuropathy and degree of QTcI prolongation in all groups examined. Thus, changes in diabetic patients appear to be attributable to CAN, rather than to diabetes per se. Evaluation of QTcI may be a simple additional diagnostic aid to identify individuals with an increased cardiovascular risk.

P1112

Cause – Effect Relationship between Hyperglycaemia and Pain Perception Threshold

ASHOK KUMAR DAS, G.R.K. Sharma, Ramaswamy S., *Medicine, Jipmer, Pondicherry, India*

Introduction: Diabetes Mellitus is commonly associated with painful neuropathy. This is effectively managed by achieving good glycaemic control.

Aim: To identify a cause – effect relationship between changes in the glycaemic status and pain threshold using clinical and experimental models.

Methods: Hyperglycemia was induced chemically in rats using streptozotocin. Assessment of pain threshold was made by thermal (tail flick) and mechanical (tail clip) assay. Clinically, the ischaemic and cold pain threshold and latency for intolerance to pain threshold (IPT) were measured in diabetic patients and healthy volunteers by tourniquet test and visual analog scale).

Results: In animal experiments hyperglycemia (from 55.17 to 118.67 mg%) decreased the reaction time from 14.9 to 8.3 seconds indicating hyperalgesia in hyperglycaemic states. This was reversed when blood sugar reduced from 118.67 to 63.7 mg%. The reaction time return almost to normal (8.89 to 17.25 seconds) on achieving glycaemic control (63.75 mg%). In humans an increase in blood glucose postprandially from 80.1 to 153.2 mg% decreased the Ischemic pain threshold (IPT) from 34.5 to 21.3 seconds. Similarly in untreated diabetic patients (323.3 mg% glucose) the IPT latency was 12.37 seconds and it returned to normal (30.87 sec.) on achieving good glycaemic control (110.93 mg%).

Conclusion: An inverse relationship exists between glycaemic status and pain threshold. It is advised to employ ischaemic pain test for constant results in humans. Inclusion of assessment of pain threshold along with other battery of tests will assist early diagnosis of painful diabetic neuropathy.

P1113

Prevalence of Neuropathy Using Biothesiometry in a Selected South Indian Population - The Chennai Urban Population Study (CUPS)

M. RAMU, G. Premalatha, R. Deepa, V. Mohan. *Madras Diabetes Research Foundation, Chennai, India*

Objective: The aim of this study was to determine the prevalence and risk factors for neuropathy among South Indians.

Methods: The Chennai Urban Population Study (CUPS) is an epidemiological study involving two residential areas in Chennai in South India. Of the total of 1399 eligible subjects (age ≥ 20 years), 1262 (90.2%) participated in the study. All the study subjects underwent a glucose tolerance test (GTT) and were categorized as normal glucose tolerance (NGT) impaired glucose tolerance (IGT) or diabetes. Biothesiometry studies were performed by a single observer using a biothesiometer

(Biomedical Instrument, Newbury, Ohio, U.S.A.) on 50% of the study subjects ($n=631$). Neuropathy was diagnosed if the vibratory threshold of the great toe exceeded 20.

Results: The overall prevalence rate of neuropathy was 7.7% (age standardised-3.9%). The prevalence rates of neuropathy were 5.8%, 14.7% and 17.5% in those with NGT, IGT and diabetes respectively. Univariate regression analysis revealed age and diabetes as strong risk factors for neuropathy ($p < 0.001$).

Conclusion: The overall prevalence of neuropathy in this urban South Indian population is 7.7% and age and diabetes are the risk factors for neuropathy. This is the first population based study on neuropathy from South Asia.

P1114

Normal Values of Parameters of Power Spectral Analysis of Heart Rate Variability for Clinical Evaluation of Autonomic Neuropathy

J. HOSOVÁ, A. Jirkovská, P. Bouček, J. Skibová. *Institute for Clinical and Experimental Medicine, Prague, Czech Republic*

Background and Aims: Diabetic cardiovascular autonomic neuropathy (CAN) carries an increased risk of mortality. Power spectral analysis (PSA) of heart rate variability (HRV) is more sensitive method for evaluating CAN than standard Ewing's battery of cardiovascular autonomic function tests. The aim of the study was to select the optimal parameters of PSA of HRV and to establish their normal age-related values. **Material and Methods:** We tested 123 healthy subjects (aged 20-70 years) with normal Ewing's tests. Short-term PSA of HRV was performed in modified orthostatic load (3x5 min, in positions supine-standing-supine), using a telemetric system VariaCardio TF4 (Sima Media, Olomouc, Czech Republic). Examination conditions were strictly standardised. **Results:** Optimal parameters of HRV within PSA were selected by stepwise discriminant analysis between groups with various stages of CAN as assessed by the battery of Ewing's tests. Cumulative spectral power of the total frequency band (0.05-0.50 Hz) in all three positions (CumPower LFHF 1+2+3) or in positions 2+3 (CumPower LFHF 2+3) were the most relevant parameters for discrimination between healthy subjects and group with severe CAN. Spectral power of low-frequency band (0.05-0.15 Hz) in all three positions (Power LF 1+2+3) was the most discriminating parameter between healthy subjects and group with early CAN. Group of healthy subjects was divided into 4 age-decades. In each age-decade was expressed the mean \pm SD for selected optimal parameters of PSA of HRV. The age-related lower limits of normal were defined at the 5th centile for severe CAN and 20th centile for early CAN. A log transformation of the data yielded linear regression between age and the corresponding SD for selected parameters: In CumPowerLFHF 1+2+3 ($r = -0.63$, $p < 0.001$), In CumPowerLFHF 2+3 ($r = -0.64$, $p < 0.001$), In Power LF 1+2+3 ($r = -0.52$, $p < 0.001$). **Conclusion:** Normal values of parameters of PSA of HRV with sufficient sensitivity can be used for diagnosis of CAN.

P1115

Simple Screening Tests for Peripheral Neuropathy in the Diabetes Clinic

B.A. PERKINS¹, D. Olaleye², B. Zinman³, V. Bril³. ¹ Harvard Medical School, Boston, United States of America; ² SAS, Carey, United States of America; ³ University of Toronto, Toronto, Canada

Purpose. The utility of rapid and valid sensory tests appropriate for diagnosis of neuropathy in the diabetes clinic, rather than as prognostic tools for the prediction of foot complications, has been unclear due to limitations inherent in previous studies. Although clinical practice guidelines recommend annual screening for neuropathy, they are unable to support specific recommendations for screening maneuvers. The objective of this study is to assess the operating characteristics of four simple sensory tests in the diagnosis of distal symmetrical polyneuropathy.

Methods. The 10 g Semmes-Weinstein monofilament examination (SWME), superficial pain sensation, vibration testing by the *on-off method*, and vibration testing by the *timed method* were assessed in 478 subjects with independent, blinded evaluations compared against the criterion standard of nerve conduction studies (NCS) in a descriptive, cross-sectional study design.

Results. The four maneuvers reveal similar operating characteristics. Cut-off points by the receiver-operating characteristic (ROC) curve analyses reveal that a "positive" or "abnormal" test is represented by ≥ 5 incorrect responses out of 8 stimuli applied and a "negative" or "normal" test is defined by ≤ 1 incorrect responses out of 8 stimuli applied. By these criteria, the point estimates of the positive and negative likelihood ratios are summarized in Table 1:

	≥ 5 out of 8 attempts insensate	≤ 1 out of 8 attempts insensate
Examination Maneuvre	(Positive LR)	(Negative LR)
Vibration (on-off)	26.6	0.51
SWME	10.2	0.34
Superficial pain	9.2	0.50
Vibration (timed)	18.5 ¹	0.33 ²

¹ Abnormal timed vibration defined as ≥ 20 seconds persistence of vibration per toe. ² Normal timed vibration defined as ≤ 10 seconds persistence of vibration per toe.

The screening tests showed comparable sensitivity and specificity results as assessed by the areas under the curve (AUC) for the ROC curves.

Conclusions. Annual screening for diabetic neuropathy should be conducted using superficial pain sensation testing, SWME, vibration testing by the *on-off method* or the *timed method*. The reported operating characteristics for each sensory modality can be applied, according to Bayes' Theorem, to positive findings on the physical examination of individual patients to predict the likelihood of neuropathy.

P1116

Early Neuropathy and Biochemical Markers of Endothelial Dysfunction in Young Diabetic Subjects

N.B. BHOWMIK¹, S. Parveen¹, A. Haque², H. Mahtab¹, A. Rahman³, L. Ali¹. ¹ Research Division, BIRDEM, Dhaka, Bangladesh;

² Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh;

³ Combined Military Hospital, Dhaka, Bangladesh

Taking advantage of a unique group of young diabetic patients in Bangladesh who are severely hyperglycemic (fasting blood glucose usually >16 mmol/l), and normo- to hypoinsulinemic without being ketotic we have studied a group of newly diagnosed, neurologically asymptomatic subjects to explore the earliest neuropathic changes in a relatively acute severe hyperglycemic condition through assessing peripheral nerve functions along with early biochemical markers of endothelial dysfunction. Thirty-two diabetic patients were studied along with 30 age- and BMI-matched control subjects. Endothelial dysfunction was estimated by serum levels of tissue plasminogen activator (t-PA), Endothelin-1 (ET-1) and von Willibrand factor (vWF). Nerve functions were evaluated by determination of distal latency (DL), compound muscle action potential (CMAP), F wave latency (FWL) and motor nerve conduction velocity (MNCV) of Ulnar and Peroneal nerves and by DL, sensory nerve action potential (SNAP) and sensory nerve conduction velocity (SNCV) of Ulnar and Sural nerves. Significant differences were observed between diabetic vs control groups regarding MUCMAP, MUFWL, MUNCV, MPCMAP, MPNCV, and SSNCV. A highly significant negative correlation was seen between the latency period and NCV. In diabetic patients blood glucose and fructosamine levels showed strong correlation with MPNCV and MUNCV. Significant differences were also observed between diabetic vs control groups regarding t-PA and ET-1. vWF failed to show any significant difference. Taking M+2SD value of Peroneal F wave latency of control subjects as cut off point 17 (53.2%) diabetic patients had prolonged F wave latency and were considered to have subclinical neu-

ropathy. Significant high t-PA values was found in the neuropathic group. The other two markers did not show any difference. The results suggest that the abnormalities of nerve functions are detected early in young diabetic subjects with motor nerve conduction parameters and F wave latencies being early to be involved. The data also suggest that t-PA may be an early predictor of neuropathy in these subjects.

P1117

Loss of Protective Sensation (LOPS) in NIDDM: Pathogenetic Association with Atherosclerosis and Nephropathy?

S.R. KRISHNAIENGAR, S. Suma, J. Hegde, N.C. Basavaraju, D.V. Rama, M.A. Srilakshmi, S. Joshi, A.S. Vinaya, G.S. Narayan, U. Dayashankar, B.S. Sudha, A.H. Mamatha, G. Raja, T. Kalpana, N. Sumithra, N. Ishrath, J. Srikanth, B.A. Mahesh, S.S. Srikanta, A. Sharda. *Samatvam Endocrinology Diabetes Center, Bangalore, Karnataka, India*

Both metabolic and hypoxic - ischemic mechanisms have been proposed to contribute to the pathogenesis of diabetic peripheral neuropathy (DPN). LOPS reflecting DPN (distal symmetric sensory) is a critical predisposing factor responsible for diabetic limb loss. 134 consecutive subjects with NIDDM, as part of their annual health review, were prospectively screened for LOPS (Semmes-Weinstein monofilament test). Ankle brachial index (ABI) was measured using a portable hand held doppler and urinary albumin excretion (UAE) by immunoturbidometry.

Parameter	LOPS (+)	LOPS (-)	P value
N(%)	9 (8)	110 (92)	
AGEDM(Y)	40	47	0.04
DMDUR(Y)	19	9	0.0002
HTN(%)	78	51	0.11
IHD(%)	56	22	0.03
CVD(%)	22	1	0.01
RETIN(%)	11	8	0.6
NEPHR(%)	44	6	0.00007
UMALB(MG/24H)	281	78	0.03
PVD(%)	78	21	0.00000
ABIWORST	0.56	0.91	0.0002

LOPS was significantly associated with early age at diabetes diagnosis (AGEDM), increasing diabetes duration (DMDUR), unequivocal ischemic heart disease (IHD), cerebrovascular disease (CVD), overt nephropathy (NEPHR), and peripheral vascular disease (PVD). The most striking observation of this study was the association of LOPS with PVD, quantitatively expressed as 'ABIWORST' (lowest of the ABI of the 4 distal vessels). Also LOPS(+) subjects had significantly higher microalbuminuria (UMALB). Conclusions: The strong association of LOPS with PVD and nephropathy, suggests possible roles for macro- and micro-vascular disease in the pathogenesis of DPN (hypoxic - ischemic mechanisms). Also, these correlations may be coincidental to common risk factors and determinants.

P1118

Insulin Resistance, Hyperinsulinaemia and Salt Sensitivity of Blood Pressure in Obese Subjects with Borderline Hypertension

LILIANA MAJKOWSKA, Piotr Moleda, Romuald Bohatyrewicz, Barbara Krzyzanowska, Stanisław Czekalski, Krystyna Pilarska. *Dept of Endocrinology and Metabolic Diseases, Pomeranian Academy of Medicine, Szczecin, Poland*

Aim of study: to evaluate the relationship between insulin resistance, hyperinsulinaemia and salt sensitivity of blood pressure in obese subjects with borderline hypertension.

Material and methods: investigated group consisted of 41 obese, newly diagnosed, untreated borderline hypertensive subjects - 11 newly diag-