

### 5.2 Pancreatic $\beta$ cell function, insulin resistance and glycaemic control in newly referred Hong Kong Chinese diabetic patients

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In 1996, we conducted a cross-sectional study on all newly referred type 2 diabetic patients to the diabetes clinic at the Prince of Wales Hospital. This is a university tertiary referral center serving a population exceeding 1.2 million. Assessment was modified from the Europe DiabCare Database and included documentation of all demographic data, treatment history, cardiovascular risk factors, micro- and macro-vascular complications. Data are expressed as mean $\pm$ SE and analysed using the ANOVA model.

Of the 562 consecutive patients, 57% were women and 43% were men with a mean age of  $54 \pm 0.6$  years (range 17-87) and a mean duration of disease of  $5 \pm 0.25$  years. At the time of referral, 70% were on drug therapy (9% on insulin and 62% on oral agents), 20% were on diet and 9% had not received treatment. The mean HbA1c was  $8.4 \pm 0.1\%$ . Insulin resistance (IR) was calculated using the homeostasis model assessment (HOMA) based on a product of fasting plasma glucose and insulin concentrations. The mean IR was  $7.39 \pm 0.46$  (range: 0.63-162.7) and correlated only with central obesity as represented by the waist hip ratio (WHR,  $p=0.008$ ). HbA1c was correlated positively with age ( $p=0.013$ ), duration of disease ( $p<0.001$ ), IR ( $p<0.001$ ) and negatively with BMI ( $p<0.001$ ). HbA1c was lower in patients who have seen dietician ( $p<0.001$ ) or specialist diabetes nurse before ( $p<0.001$ ) or who performed self blood glucose monitoring ( $p=0.001$ ). HbA1c was higher if the patients were smokers ( $p=0.003$ ). We defined insulin deficiency as a fasting plasma C-peptide  $<0.2$  pmol/L. Compared to insulin deficient patients ( $n=118$ ), non insulin deficient patients ( $n=413$ ) had features of the metabolic syndrome with increased WHR ( $p=0.005$ ), blood pressure ( $p<0.001$ ), body mass index ( $p=0.001$ ) and were older ( $p=0.04$ ). Amongst the insulin deficient patients, 27% were treated with oral agents or diet. Patients were considered to be on appropriate treatment if insulin-deficient patients were treated with insulin or non-insulin deficient patients, treated with oral drugs. Patients receiving appropriate therapy ( $n=362$ ) had a lower HbA1c than those treated inappropriately ( $n=173$ ) ( $8.2\%$  vs  $8.7\%$ ,  $p=0.02$ ). On multivariate analysis, duration of disease ( $p<0.001$ ), IR ( $p=0.008$ ) and BMI ( $p=0.012$ ) were the major determinants of glycaemic control. Our findings confirmed the heterogeneity of pancreatic  $\beta$  cell function and insulin resistance in Chinese type 2 diabetic patients. Non-insulin deficient patients exhibited features resembling the metabolic syndrome. Many insulin deficient patients were treated with diet or oral drugs. Appropriate therapy in relation to pancreatic  $\beta$  cell function was associated with improved glycaemic control. Our findings emphasize the importance of documenting insulin secretory function and actions in Chinese diabetic patients, which influence the efficacy of therapy. We also demonstrated the importance of patient education by specialist nurse and dietician, self monitoring, life style factors especially smoking and choice of appropriate modality of therapy in determining glycaemic control.

### 5.3 Sputum elastase activity correlates with clinical parameters in steady state bronchiectasis

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**Objectives:** Bronchiectasis is a largely idiopathic disease whereby patients suffer from regular sputum production and recurrent exacerbations. Sputum from patients with bronchiectasis contains a large number of toxic substances which originate from the colonising bacteria such as *Pseudomonas aeruginosa* and also the host such as leucocyte elastase. The role of elastase in the pathogenesis of bronchiectasis has long been suggested although there has never been any systematic studies to evaluate its correlation with clinical parameters. We have therefore measured the sputum elastase activity and correlate this with clinical parameters in patients with steady state idiopathic bronchiectasis.

**Methods:** Thirty patients (17F;  $48.5 \pm 16.5$  yrs; FEV<sub>1</sub>/FVC  $1.3 \pm 0.6/2.1 \pm 0.9$ ) who were in were recruited. 24h sputum volume, and purulence and viscosity scores were assessed for each patient. Freshly produced sputum was obtained after physiotherapy to obtain the sol phase after ultracentrifugation at 4°C and 100,000g. Elastase level was measured by using spectrometry and digestion of a chromogenic peptide. Sputum sol phase interleukin (IL)-1 $\beta$ , IL-8, tumor necrosis factor (TNF), and leukotriene (LT) B<sub>4</sub> were measured using ELISA techniques.

**Results:** There was significant correlation between purulence score and 24h sputum volume, *Pseudomonas aeruginosa* (PA) density, IL-1 $\beta$  and TNF levels, and sputum leucocyte density ( $p<0.02$ ). IL-1 and IL-8 levels correlated with sputum leucocyte density ( $p<0.04$ ). There was correlation between elastase levels with 24h sputum volume, FEV<sub>1</sub>, FVC, number of bronchiectatic lung lobes, and sputum leucocyte density ( $p<0.05$ ).

**Conclusions:** The results of this study provide original quantitative evidence to suggest the important role of neutrophil elastase in the pathogenesis of bronchiectasis. Further novel therapies against elastase should be devised and tried in patients with bronchiectasis.