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Title	Impaired glucose tolerance as a risk factor for diabetes mellitus and hypertension in the Hong Kong Chinese population: a 5-year prospective study
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Impaired glucose tolerance as a risk factor for diabetes mellitus and hypertension in the Hong Kong Chinese population: a 5-year prospective study

Key Messages

1. The conversion rate to type 2 diabetes at 5 years was 20% among Chinese subjects with impaired glucose tolerance, which was 8-fold that of sex- and age-matched normal controls.
2. Body mass index, fasting and 2-hour plasma glucose predicted type 2 diabetes risk.
3. Cumulative prevalence of hypertension was consistently higher among subjects with impaired glucose tolerance than in those with normal glucose tolerance. Age, systolic blood pressure, and body mass index were predictive factors of incident hypertension in this study cohort.
4. Based on our cohort, the sensitivity and specificity of the Asian cut-off values for overweight and central obesity, recommended by the World Health Organization for identifying subjects at risk of diabetes and hypertension, appeared more appropriate for our population than values advocated for Caucasians.

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Introduction

Type 2 (non–insulin-dependent) diabetes mellitus (NIDDM) is associated with increased cardiovascular and all-cause mortality due to accelerated atherosclerosis. This increased cardiovascular risk, secondary to the underlying insulin resistance,[1] probably precedes the onset of diabetes. Besides having a known pre-diabetic state, non-Chinese subjects with impaired glucose tolerance (IGT) have been reported to be at substantial risk of developing cardiovascular and cerebrovascular diseases.

Well-designed randomised controlled studies have demonstrated the impact of lifestyle measures in individuals with IGT on progression to diabetes mellitus (DM).[2,3] In order to study the incidence of, and predictive factors for, the development of type 2 DM in the local Hong Kong Chinese population with IGT, we prospectively followed up a cohort of 434 IGT subjects, and age- and sex-matched normal controls, identified from a community-based population study in 1996 and 1997.

According to the World Health Organization (WHO) 1998 criteria,[4] diabetes is defined by a fasting plasma glucose (FPG) of ≥ 7 and/or a 2-hour plasma glucose of ≥ 11.1 mmol/L, and IGT by a 2-hour plasma glucose of ≥ 7.8 mmol/L but <11.1 mmol/L, in subjects with a FPG of <7 mmol/L.

Aims and objectives

The aims of this study were:
1. To determine the conversion rate of IGT to type 2 diabetes, as compared to normal subjects, within 5 years using the WHO[4] (1985 and 1998) diagnostic criteria[5];
2. To ascertain the prevalence and incidence of increased blood pressure (BP) [systolic ≥ 140 mm Hg and/or diastolic ≥ 90 mm Hg] as well as its associations with other cardiovascular risk factors at 5 years, among IGT as compared to normal subjects; and
3. To determine the cumulative incidence of both coronary heart disease and stroke among IGT as compared to normal subjects at 5 years.

Methods

This study was conducted from September 2000 to August 2002. Four hundred and thirty-four subjects with IGT were identified from a local community-based study,[6] which began in January 1995. One major objective of the study was to assess the prevalence of type 2 diabetes and IGT in the local Chinese population. Baseline demographic, anthropometric, and biochemical data were collected. The IGT subjects were invited to participate in a 5-year follow-up study. An equal number of subjects with normal glucose tolerance (NGT), matched for age and sex, were also recruited from the same source to serve as controls. These NGT subjects and all subjects with IGT at baseline were invited to return for a face-to-face interview and repeat of the oral glucose tolerance test 5 years later.

Table 1. Conversion to type 2 diabetes mellitus within 5 years (based on World Health Organization 1998 diagnostic criteria)*

Status at baseline	Status at 5 years			Total
	NGT	IGT	DM	
NGT	254 (79.9%)	56 (17.6%)	8 (2.5%) [95% CI: 0.8-4.2%]	318 (100%)
IGT	107 (39.5%)	110 (40.6%)	54 (19.9%) [95% CI: 15.2-24.6%]	271 (100%)
Total	361	166	62	589

* NGT denotes normal glucose tolerance, IGT impaired glucose tolerance, and DM diabetes mellitus

Table 2. Anthropometric adiposity variables, stratified by gender and glycaemic status (as defined by the World Health Organization 1998 diagnostic criteria) at 5 years

Anthropometric characteristic	Glycaemic status at 5 years*		F	P value[†]
	DM (n=62)	Non-DM (n=527)		
Waist circumference (cm)				
Men	88.35±7.01	84.32±9.24	1.09	0.004
Women	84.31±8.66	76.82±8.72	0.01	<0.001
Body mass index (kg/m²)				
Men	26.85±2.76	24.34±3.46	0.89	<0.001
Women	27.51±3.15	24.58±3.85	1.30	<0.001
Waist-hip ratio				
Men	0.92±0.06	0.89±0.07	0.765	0.031
Women	0.86±0.06	0.81±0.07	0.772	0.002

* DM denotes diabetes mellitus
[†] Independent Student's *t* test

Height was measured to the nearest 0.5 cm and weight to the nearest 0.1 kg. Participants were measured in socks, stockings, or bare feet and light street clothing (no coats or jerseys). Body mass index (BMI) was calculated as weight/height². Waist and hip circumferences were measured twice to the nearest 0.5 cm and the means were used for subsequent analyses. Waist circumference was measured half-way between the xiphisternum and the umbilicus while hip circumference was measured at the level of the greater trochanters.

Blood pressure was measured sitting at rest, using fifth phase sounds with a mercury sphygmomanometer. Hypertensive subjects were defined as those taking anti-hypertensive agents and those with untreated systolic BP of ≥140 mm Hg and/or diastolic BP of ≥90 mm Hg.

Results

A total of 271 IGT (response rate, 62%) and 318 NGT (response rate, 73%) subjects returned at 5 years for re-study. The baseline characteristics of the non-participants (n=163) were not significantly different from the participants, except for higher triglyceride levels. Among the NGT subjects, those who returned were significantly older, having higher 2-hour plasma glucose levels, systolic and diastolic BPs, and were more obese than those who did not.

Anthropometric and biochemical data were analysed among the 271 IGT subjects and their age- and sex-matched NGT controls (IGT+NGT: n=589). At baseline, IGT subjects as a group had significantly higher values for: BMI, waist circumference, waist-hip ratio, total blood cholesterol, low-density lipoprotein–cholesterol, triglyceride, fasting and 2-hour plasma glucose, systolic and diastolic BPs, but they had lower high-density lipoprotein–cholesterol levels.

Of the 271 IGT subjects, 54 (19.9%; 95% confidence interval [CI], 15.1-24.7%) progressed to diabetes, 110 (40.6%) still had IGT only, and 107 (39.5%) reverted to NGT. Of those in the NGT group, 8 (2.5%; 95% CI, 0.8-2.8%) progressed to diabetes, 56 (17.6%) were reclassified as having IGT, and 254 (79.9%) as NGT. Using the WHO (1998) diagnostic criteria, the conversion rate to type 2 diabetes among IGT and NGT subjects at 5 years was 20% (ie 4% per year on average) and 2.5% respectively (Table 1). Each of the obesity markers at baseline predicted diabetes at 5 years (Table 2). Conversion to diabetes at the 5-year follow-up was predicted by baseline fasting glucose, post-load 2-hour plasma glucose and BMI, using the multiple logistic regression analysis forward stepwise method.

Baseline hypertension prevalence among IGT subjects (30%) was significantly higher than in NGT subjects (22%) [P=0.016]. This difference in the cumulative prevalence of hypertension between IGT and NGT subjects remained at 5 years (IGT 47% vs 38%, P=0.028). Among normotensive subjects at baseline, 18% (80/437) had developed hypertension within 5 years. Age, systolic BP, and BMI at baseline were significant predictors of incident hypertension at 5 years.

Body mass index could serve as a screening tool for diabetes and hypertension, using lower Asian-specific cut-

off values for normality (23 kg/m^2), in contrast to the higher general cut-off value (25 kg/m^2) advocated by the WHO. Improved detection sensitivity (men: 90% vs 74%; women: 100% vs 74%) and specificity (men: 65% vs 41%; women: 63% vs 39%) were observed.

Only 20 subjects in the IGT cohort developed cardiovascular and/or cerebrovascular end-points over the 5-year study period. The numbers were too few for any conclusion to be drawn regarding the cardiovascular risk conferred by IGT.

Discussion

Our 5-year prospective study has demonstrated a significantly higher risk of progression to type 2 diabetes in Chinese subjects with IGT (20% over 5 years, or 4% per year, based on WHO 1998 diagnostic criteria), as compared to normal controls. Although differential response rates among IGT and NGT subjects might reflect their respective motivations for returning, the distribution of answers to questions administered at 5 years and at baseline showed a high degree of consistency.

Individually, each of the parameters of overall or central obesity can independently predict diabetes. However, baseline FPG, 2-hour plasma glucose and BMI were significant predictors of diabetes at 5 years, after adjusting for other significant baseline variables. As waist circumference and waist-to-hip ratio are highly correlated (r=0.80; P<0.001), practicality comes into the picture. Since waist circumference is much simpler to determine than waist-to-hip ratio, both in day-to-day clinical practice or in epidemiological surveys, the former marker is preferred in assessing central obesity with regard to diabetes risk. Increasing BMI is associated with a higher risk of diabetes, hypertension, and other cardiovascular risks in both Caucasians and Asians. Our data using the development of diabetes or hypertension within 5 years as markers of obesity-related co-morbidities, suggest that lower cut-off values for both BMI (25-23 kg/m^2) and waist circumference (men: 102-90 cm; women: 88-80 cm) be recommended for Asians, to improve detection sensitivity although it reduces specificity. As a screening tool for increased risk of developing diabetes or hypertension, BMI is more sensitive but less specific than waist circumference. Among subjects who were normotensive at baseline, age, systolic BP, and BMI were significant predictors of incident hypertension after 5 years.

Our study has confirmed the increased risk of diabetes and hypertension associated with IGT. Current practice in its detection and management is probably inadequate and needs to be reviewed, taking into consideration factors predictive of the development of diabetes and hypertension identified in our population.

Conclusions

The 5-year cumulative diabetes conversion rate among IGT subjects in Hong Kong was eight times that of age- and sex-matched NGT controls. At baseline, IGT subjects as a group had more unfavourable cardiovascular risk factors than NGT subjects. We found that BMI, together with the fasting and 2-hour plasma glucose, predicted type 2 diabetes, and when used together with age and systolic BP, it could also predict hypertension. Using development of diabetes or hypertension at 5 years as markers of obesity-related co-morbidities, our data suggest that lowering BMI and waist circumference cut-off levels recommended for Asians, can improve the detection sensitivity and reduce the specificity for these diseases. Body mass index is more sensitive as a screening tool than waist circumference.

Acknowledgement

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