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# Central Rather than Generalized Obesity is Related to Hyperglycaemia in Asian Indian Subjects

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> The relationship of body mass index and waist-hip ratio with plasma glucose concentrations during an oral glucose tolerance test (OGTT) was studied in native Indian (Asian) subjects. A total of 389 subjects (131 non-diabetic, 74 impaired glucose tolerant (IGT) and 184 Type 2 diabetic (newly diagnosed and untreated)) were studied. Prevalence of obesity  $(BMI \ge 27.0 \text{ kg m}^{-2} \text{ in men and} \ge 25.0 \text{ kg m}^{-2} \text{ in women, } 21 \% \text{ and } 47 \%, \text{ respectively})$ was lower in people with Type 2 diabetes than that reported in white Caucasian and migrant Asian populations. Body mass index was highest in IGT subjects (26.1 (19.7-34.3) kg m<sup>-2</sup>, median (5-95th centile)) and was higher in diabetic subjects (24.2 (19.3-32.2) kg m<sup>-2</sup>) than in non-diabetic control subjects (23.5 (17.1-30.0) kg m<sup>-2</sup>). However, waisthip ratio was higher in both IGT (0.88 (0.75-0.98)) and diabetic subjects (0.88 (0.75-1.00)) than in non-diabetic control subjects (0.83 (0.70-0.97)), with no difference between the hyperglycaemic groups. On multivariate analysis, fasting as well as 2-h plasma glucose concentrations during OGTT were found to be related to waist-hip ratio (p < 0.01) and subscapular fat thickness (p < 0.01) but not to body mass index (or triceps fat thickness). Thus, in native Indians central obesity seems to be a more important association of hyperglycaemia than generalized obesity.

KEY WORDS Glucose tolerance Asian Indians Central obesity Waist-hip ratio
Type 2 diabetes Impaired glucose tolerance

#### Introduction

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Type 2 diabetes is the predominant type of diabetes in Asian Indians¹ with a high prevalence in migrant²-⁴ as well as native Asians.⁵-₹ Relatively young age at onset, strong familial aggregation, and relative lack of obesity are notable features of Type 2 diabetes in Asians.<sup>8,9</sup> The high morbidity due to coronary artery disease amongst migrant Asian subjects is thought to be related to higher prevalence of diabetes in migrant Asians¹0-14 compared with native populations. Type 2 diabetes and coronary artery disease have been been suggested to be a consequence of insulin insensitivity,¹5 present amongst Asians even in the absence of obesity.

Distribution of body fat (upper segment rather than lower segment, central rather than generalized, 'android' rather than 'gynoid') is thought to be more important than the mere presence of obesity in having metabolic consequences such as insulin insensitivity and diabetes, hyperlipidaemia, and atherosclerosis. <sup>16–22</sup> There is no information on the prevalence of central obesity and its relationship with diabetes and other problems in native Indian (Asian) subjects. We have therefore measured generalized obesity (as body mass index) and central obesity (as waist-hip ratio) in newly diagnosed hypergly-caemic native Asian subjects and in non-diabetic control

subjects to study the relationship between obesity and plasma glucose concentrations during an oral glucose tolerance test.

#### Patients and Methods

The Wellcome Diabetes Study is a prospective study from diagnosis of the clinical, biochemical, and endocrine features of native Indian diabetic patients at the King Edward Memorial Hospital, Pune, India. This hospital serves middle and poor socio-economic class populations of the city and adjoining district.

Newly diagnosed, untreated hyperglycaemic subjects were enrolled serially over 2 years from the outpatients and wards. The following categories of subjects were excluded: age > 65 years; pregnant women; people with cancer; recent (within 6 months) invocardial infarction or stroke; other severe illnesses; and those on steroid treatment. Approximately 10 % of eligible subjects declined to participate in the study. Non-diabetic control subjects had either been outpatients for various minor illnesses (99), or were spouses of patients (16) or hospital staff (16). None of these had a family history of diabetes or symptoms of pancreatic disease. Subjects with impaired glucose tolerance (IGT) comprised 40 outpatient subjects who volunteered for an OGTT (including 9 spouses) and 34 referred to us for an OGTT because of at least one symptom commonly associated with diabetes (polyuria,

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polydipsia, polyphagia, weight loss or genital symptoms) and/or a family history of diabetes.

A 75 g oral glucose tolerance test (OGTT) was performed after an overnight fast. Blood samples were obtained via a cannula in an antecubital vein. Two baseline samples were averaged to give fasting glucose value. Plasma glucose (glucose oxidase) was measured on an Abbot VP Super autoanalyser (Irving, TX, USA) using the standard kit. Glycosylated haemoglobin (HbA<sub>1</sub>) was measured by a colorimetric method,<sup>23</sup> normal 4.3–8.0 %.

The following anthropometric measurements were recorded at the time of OGTT: height, weight, triceps skinfold thickness at a point midway between the acromion and the lateral epicondyle of humerus, and subscapular skinfold thickness just below the scapula, both with skin calipers (Timesco, London, UK). Minimum circumference of waist between the lower margin of rib cage and the highest point of iliac crest and the maximum circumference of hips near the level of the greater trochanters were measured, both with subjects standing comfortably, arms hanging by side and normal respiration, in comfortable indoor clothing. All measurements were taken by one of the two observers using the same equipment. There was good agreement between the two observers and between two measurements made by the same observer (CV < 5 % for all anthropometric measurements). Obesity was defined ≥ 27.0 kg m<sup>-2</sup> in men and ≥ 25.0 kg m<sup>-2</sup> in women.<sup>24</sup>

Data on a total of 389 subjects is presented. Subjects were classified as non-diabetic (131, 73 men), impaired glucose tolerant (IGT) (74, 42 men), and diabetic (184, 118 men) according to the WHO (1985) criteria for 2-h plasma glucose during OGTT. Diabetic subjects fulfilled the criteria of non-insulin-dependent, Type 2 diabetes (WHO, 1985) and have now been followed for a minimum of 2 years. One-hundred and thirty-one (71 %) diabetic subjects complained of at least one symptom commonly associated with diabetes (see above); others were asymptomatic. Sixty-nine (38 %) diabetic and 7 (10 %) IGT subjects gave a history of weight loss before diagnosis, though the actual loss was known to only a few. Fourteen (8 %) diabetic and 12 (16 %) IGT subjects admitted to having gained weight in the recent past. Socio-economic classification of subjects showed that 11 % of non-diabetic, 4 % of IGT, and 13 % of diabetic subjects could be classified as poor (admitted total family income < Rs 1000 per month), 53 % of non-diabetic, 36 % IGT, and 49 % diabetic as lower middle class (Rs 1000-3000 mo-1) and 39 % of non-diabetic, 60 % of IGT, and 38 % of diabetic as belonging to upper middle class (> Rs 3000 mo-1). Thus, the IGT group had a significantly higher percentage of people from the upper socio-economic class (p < 0.05, compared with both other groups).

Statistical analysis was by non-parametric tests (Mann-Whitney U test, Spearman's rank correlation coefficient). Multivariate analysis was by multiple linear regression analysis on data 'normalized' by logarithmic transformation whenever necessary.

#### Results

Table 1 shows the basic clinical features of different groups. Non-diabetic men were younger than IGT men (p < 0.01); non-diabetic women were younger than diabetic women (p < 0.05). Plasma glucose and HbA<sub>1</sub> concentrations showed the expected differences between the groups.

In both sexes, subjects with IGT were the most obese by BMI criteria. Comparison between groups showed that BMI was similar in non-diabetic and diabetic men, but men with IGT had a greater BMI than either nondiabetic (p < 0.01) or diabetic men (p < 0.05). Nondiabetic women had a lower BMI than women with either IGT (p < 0.001) or diabetes (p < 0.05), while women with IGT had greater BMI than did diabetic women (p < 0.05). Thirty-one percent of men with IGT were obese compared with 15 % of non-diabetic subjects (p < 0.05), while the percentage in the diabetic group (21 %) was not significantly different from the other two groups. Seventy-five percent of women with IGT were obese compared with 39 % non-diabetic women (p < 0.01), and 47 % of diabetic women (p < 0.01); there was no significant difference between non-diabetic and diabetic women.

Non-diabetic men and women both had a smaller waist-hip ratio than subjects of the same sex with IGT and diabetes (p < 0.01, all). There was no difference between IGT and diabetic subjects.

The distribution of BMI and waist-hip ratio in different study groups is shown in Figure 1. Waist-hip ratio showed a clear 'shift to the right' in both IGT and diabetic subjects, which differentiated them from non-diabetic subjects, while there was no significant difference in the distribution of waist-hip ratio in IGT and diabetic subjects. BMI showed a 'shift to the right' in IGT subjects compared with non-diabetic control subjects. Such a shift was not significant in the diabetic subjects.

Correlations of BMI and waist-hip ratio with other measures are shown in Table 2. When all subjects were considered together (men and women, all categories) BMI was not correlated with fasting or 2-h plasma glucose but waist-hip ratio was directly related with fasting and 2-h plasma glucose ( $r_s = 0.26$ , and  $r_s = 0.25$ , p < 0.001, both). Similar relationships were observed for both sexes separately. A closer look at the data revealed that the relationship between 2-h plasma glucose and BMI for the whole population of subjects was (inverted) parabolic, being positive in non-diabetic control subjects and IGT subjects but negative in the diabetic patients.

Multivariate analysis of 2-h plasma glucose (logged value) for the total population of subjects (non-diabetic + IGT + diabetic, men and women) revealed a significant association with waist-hip ratio (p < 0.01) allowing for

Table 1. Characteristics of the control, IGT, and diabetic subjects studied

	Non-diabetic		Impaired Gluco	se Tolerance	Diabetic		
	$     \text{Men} \\     (n = 73) $	Women (n = 58)	Men (n = 42)	Women $(n = 32)$	Men (n = 118)	Women $(n = 66)$	
Age (yr)	40 (18–65)	40 (21–59)	48 (14-65) <sup>b</sup>	45 (29–63)	43 (16–65)	45 (22-64)*	
Height (m)	1.67 (1.55-1.80)	1.53 (1.44-1.63)	1.65 (1.51-1.83)	1.55 (1.45-1.68)	1.66 (1.50-1.85)	1.54 (1.41-1.72)	
Weight (kg)	65.0 (46.0-88.0)	55.0 (36.0-79.0)	70.8 (45.0-141.0)*	66.3 (44.0-93.0) <sup>e</sup>	65.5 (39.0-97.0)	60.5 (44.0-96.0)b,d	
BMI (kg m <sup>-2</sup> )	23.3 (16.1-33.2)	23.5 (16.6-33.8)	25.9 (17.7-45.0)b	27.3 (18.8-42.5)	23.9 (14.7-34.8)d	24.9 (18.8-40.2)**	
Waist-hip ratio	0.88 (0.76-1.01)	0.77 (0.64-0.89)	0.93 (0.76-0.99)*	0.79 (0.73-0.92)h	0.92 (0.80-1.07)€	0.81 (0.70-0.93)6	
Triceps (mm)	13 (4-27)	19 (5-35)	14 (6-39)	26 (13-40) <sup>c</sup>	12 (5-25)*	20 (4-47)*	
Subscapular (mm)	24 (6-48)	27 (7-50)	34 (13-50) <sup>e</sup>	38 (16-50) <sup>c</sup>	26 (8-50)**	33 (8-50)	
Fasting plasma glucose (mmol 1-1)	4.6 (2.7-5.6)	4.6 (2.2-6.6)	5.2 (3.7-7.7) <sup>c</sup>	5.2 (4.4-6.4) <sup>c</sup>	8.9 (4.1-20.5) <sup>c,f</sup>	8.8 (4.3-16.7) <sup>c,f</sup>	
2-h plasma glucose (mmol l <sup>-1</sup> )	5.7 (2.6-7.7)	6.4 (3.2–7.6)	8.9 (7.8–10.9) <sup>c</sup>	9.2 (7.8–10.6) <sup>c</sup>	18.5 (11.2-40.2) <sup>c,f</sup>	19.1 (11.2–34.9) <sup>c,f</sup>	
HbA <sub>1</sub> (%)	6.3 (4.5-7.9)	6.3 (4.3-8.0)	6.4 (4.7-8.1)	6.7 (5.0-9.1)*	8.9 (5.0-14.0) <sup>c,f</sup>	8.6 (5.8-15.1) <sup>c,f</sup>	

\*p<0.05; \*p<0.01; \*p<0.001 compared with non-diabetic. \*p<0.05; \*p<0.01; \*p<0.001 compared with IGT.

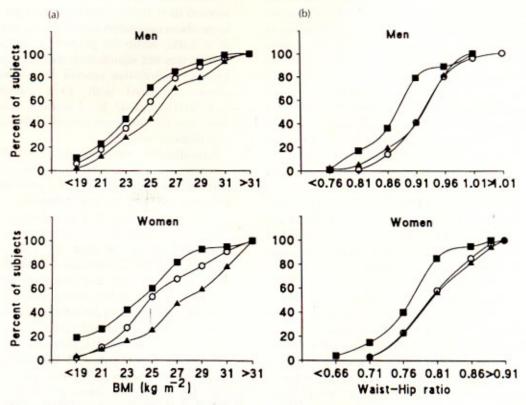


Figure 1. Frequency distribution of (a) body mass index (BMI) and (b) waist-hip ratio in nondiabetic control (■-■), impaired glucose tolerance (▲-▲), and Type 2 diabetic subjects (O-O)

interaction with age, sex, BMI, triceps, and subscapular skinfold thickness and fasting plasma glucose (logged value). Fasting plasma glucose (p < 0.001) and subscapular skinfold thickness (p < 0.01) but not BMI were also significantly related. Men showed a significant association with fasting plasma glucose (p < 0.001) and waist-hip ratio (p < 0.001), women with fasting plasma glucose subscapular (p < 0.001)and skinfold thickness (p < 0.01). The total variance explained by these parameters was ~80 %, of which ~5 % was contributed by waist-hip ratio and ~80 % by the fasting plasma glucose. Similarly, multivariate analysis of fasting plasma glucose revealed a significant association with waist-hip ratio (p < 0.001) but not BMI. However, the total variance accounted for in this equation was small at around 8 %. The interactive relationship between 2-h plasma glucose and two parameters of obesity (BMI and waist-hip ratio) is shown in Figure 2 and highlights the stronger relationship between blood glucose levels and waist-hip ratio compared with BMI for both sexes.



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Table 2. Correlations of body mass index (BMI) and waist-hip ratio with other anthropometric parameters and measures of blood glucose in the control, IGT, and diabetic subjects studied

	Non-diabetic		IGT		Diabetic		All	All	
	Men	Women	Men	Women	Men	Women	Men	Women	
BMI with:									
Age	0.13	0.20	< 0.10	0.25	< 0.10	< 0.10	0.10	0.13	0.10
Waist-hip ratio	0.59°	0.43°	< 0.10	0.26	0.34°	-0.20	0.39c	0.20ª	0.15b
Triceps	0.63°	0.85€	0.59€	0.82€	0.63°	0.61	0.62€	0.75	0.63°
Subscapular	0.75°	0.79°	0.76€	0.69€	0.75°	0.75°	0.76°	0.77°	0.78°
Fasting plasma glucose	0.14	0.16	< 0.10	0.15	-0.31°	-0.10	< 0.10	0.16*	< 0.10
2-h plasma glucose	0.34 <sup>b</sup>	0.39b	0.26	-0.46b	-0.31°	-0.10	< 0.10	0.17*	< 0.10
HbA <sub>1</sub>	< 0.10	-0.14	< 0.10	< 0.10	-0.39°	-0.17	-0.10	< 0.10	< 0.10
Waist-hip ratio with:									
Age	0.23	< 0.10	< 0.10	-0.24	0.10	< 0.10	0.20b	< 0.10	0.14b
Triceps	0.415	0.45°	-0.24	< 0.10	0.11	$-0.30^{a}$	0.14	0.13	-0.29°
Subscapular	0.50°	0.48°	< 0.10	0.19	0.29b	-0.31	0.34°	0.20*	< 0.10
Fasting plasma glucose	0.33b	0.20	0.26	< 0.10	< 0.10	0.17	0.32c	0.31°	0.26
2-h plasma glucose	0.37°	0.30	0.33a	-0.16	-0.11	0.15	0.31°	0.32€	0.25
HbA,	0.20	< 0.10	< 0.10	< 0.10	< 0.10	0.36b	0.20b	0.25b	0.22

Spearman correlation ( $r_s$ ). \*p<0.05; \*p<0.01; \*p<0.001.

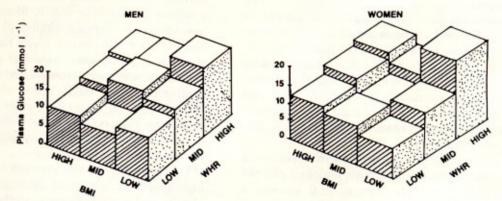


Figure 2. Mean 2-h plasma glucose concentrations during the oral glucose tolerance test in different groups of subjects divided by tertiles of BMI and waist-hip ratio (WHR) for the total population of subjects studied

#### Discussion

There are only a few large-scale population studies of anthropometric parameters and glucose tolerance in India.<sup>8</sup> Difficulties in organizing large population-based studies in developing countries are well known. Hospital-based studies suffer from an inherent bias of population selection, but they can include a greater variety of investigations and quality control is much easier. We performed extensive investigations (to be reported elsewhere) in a sizeable number of subjects attending our hospital to study various aspects of diabetes in native Indian subjects because of the increasing interest in this field in recent years. This study is expected to provide

useful guidelines for a larger population-based study of glucose intolerance and related disorders.

The present study confirms the relative lack of generalized obesity in native Indian diabetic subjects. Only 21 % of men and 47 % of women with diabetes were obese by the commonly used BMI criteria. Obesity (BMI) was related to socio-economic status and this would partly account for the higher obesity in IGT group. It is also possible that weight changes prior to diagnosis had affected BMI in some, but the numerical contribution could not be ascertained. In the Indian Council of Medical Research multicentre study<sup>8</sup> conducted approximately 15 years ago, the BMI for normal subjects of various age groups ranged from 18.9–22.8 kg m<sup>-2</sup>, indicating

relative lack of obesity in the Indian population, and only 32 % of the diabetic subjects were classified obese. Ramachandran et al.<sup>6</sup> discovered a high prevalence of Type 2 diabetes in South India but only 26 % of diabetic patients were obese by BMI criteria.

BMI in migrant Asian diabetic patients in the UK had a mean of around 25.5 kg m<sup>-2</sup> for men and around 27.0 kg m<sup>-2</sup> for women, higher than those for native Indians, but similar to those in native white Caucasians (around 26.0 kg m<sup>-2</sup> for men, around 26.5 kg m<sup>-2</sup> for women).<sup>3,4,14</sup> This possibly reflects the effect of migration to a more affluent country. It is significant that for similar BMI, the migrant Asians have a much higher risk of Type 2 diabetes than native white Caucasians. Similar observations have been made in migrant Asians in the Fiji islands.<sup>2</sup> The possible reasons for the higher risk in (migrant) Asians have become apparent only recently.

The distribution of body fat is different in men and women, men tending to accumulate it near the waist (centripetal) and intra-abdominally, while in women it is distributed around the hips (centrifugal) and subcutaneously.16 Intra-abdominal fat seems to have more effect on metabolism, and individuals with central obesity are prone to develop insulin insensitivity, glucose intolerance, hypertriglyceridaemia, and also the related disorders of hypertension and atherosclerosis. 17-22 We found that waist-hip ratio was significantly greater in subjects with IGT and diabetes compared with nondiabetic subjects of the same sex. Recent studies comparing body fat topography in migrant Asian subjects with those in white Caucasians also found a higher waist-hip ratio in migrant Asians despite comparable BMI and showed an association of waist-hip ratio with hyperglycaemia, plasma insulin concentrations, blood lipids, and coronary artery disease.25

Development of 'diabetic' hyperglycaemia requires a journey from normoglycaemia through impaired glucose tolerance. In both men and women, BMI showed a 'hump' in the IGT group which was significantly higher than in both non-diabetic and diabetic groups. Indeed, in diabetic men the BMI had 'fallen' to 'normal' levels while in women it 'fell' but was still higher than in normal control subjects. Similarly, triceps fat in men and women with diabetes was significantly lower than that in subjects with IGT. Thus, both generalized obesity and peripheral fat were lower in the more severely hyperglycaemic (diabetic) individuals, than in the less severely hyperglycaemic (IGT) subjects. It is also interesting that the relationship of BMI with plasma glucose is inverse in hyperglycaemic subjects, possibly reflecting the weight loss that accompanies marked hyperglycaemia. On the contrary, the two measures of 'central' obesity (waist-hip ratio and subscapular fat) were significantly higher in both groups of hyperglycaemic subjects than in control subjects and there was no decline in these measures with increasing hyperglycaemia. The more severely hyperglycaemic subjects thus had less peripheral but more central fat despite lower BMI. The cause and effect in this relationship cannot be commented on in a cross-sectional study like ours, but it would appear that weight loss associated with progressive hyperglycaemia is 'differential' rather than generalized or that the individuals destined to develop progressive hyperglycaemia are more centrally obese from the beginning. The primacy of the relationship between hyperglycaemia and central obesity is seen on multivariate analysis, waist-hip ratio and subscapular skinfold thickness remaining significantly associated with plasma glucose but not the BMI and triceps skinfold thickness. Figure 2 also demonstrates the steeper and more consistent gradient of hyperglycaemia in relation to increasing waist-hip ratio compared with increasing BMI. Prospective studies in French<sup>16</sup> and Swedish obese women<sup>26</sup> have highlighted the future risks of central obesity, supporting our contention. It would be informative to follow up our normal and IGT subjects prospectively to correlate changes in anthropometric parameters with changes in glucose tolerance. It is worth pointing out that the majority of previous studies in white populatic have stressed the risks of central obesity in women but in the Indian population men seem to be similarly predisposed to the risks of central obesity.

The exact mechanisms underlying the association between central obesity and metabolic disturbances are unknown. A possible link is through sex hormones.<sup>27</sup> Low serum sex-hormone-binding-globulin concentrations and high free testosterone levels have been found to be associated with higher waist-hip ratio in women and these parameters are in turn related to insulin insensitivity measured during euglycaemic clamp studies. Asian subjects are, in general, known to be more insulin insensitive than equally obese white Caucasians.<sup>28,29</sup> It is possible that central obesity plays a key role in this association.

To conclude, in this cross-sectional study we have highlighted an important association between central obesity and hyperglycaemia in otherwise relatively non-obese Indian subjects. There is a need for large (community-based) as well as prospective studies correlate anthropometric characteristics with development of glucose intolerance.

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