Original article

CLINICAL, BIOPHYSICAL AND BIOCHEMICAL VARIABLES FROM AFRICAN-HERITAGE SUBJECTS WITH TYPE 2 DIABETES

M. P. Hermans, C. Dumont, M. Buysschaert

Key words : type 2 diabetes; Bantu; ethnicity; HOMA; body fat; interprandial lipids; epidemiology.

Abbreviations : %ß: ß-cell function assessed from HOMA model; BMI: body mass index; BP: blood pressure; C: cholesterol; CCBs: calcium channel blockers; EEC: European Economic Community; GFR: glomerular filtration rate estimated by Cockroft-Gault formula; HOMA: homeostasis model assessment; IGT: impaired glucose tolerance; NGT: normal glucose tolerance; NS: non significant; RIA: radioimmunoassay; %S: insulin sensitivity assessed from HOMA model; SD: standard deviation; TG: triglycerides; WHR: waist-to-hip ratio.

ABSTRACT

We compared the metabolic profile of two ethnic populations with type 2 diabetes, one from Bantu (n=23; *Ban*) and the other from Belgian (n=314) extraction followed at St Luc Hospital. Further comparison with a Belgian sub-cohort (n=64; *Be*) matched for age (52 yrs) and sex distribution (M/F : 61/39 %) showed no significant difference between Belgian and Bantu subjects with regards to diabetes duration (9 and 11 yrs; *Ban* and *Be* respectively), age at diabetes diagnosis (43 and 42 yrs), HbA_{1c} (8.1±1.9 *vs.* 8.5±1.9 %; *NS*), and achieved education level. BMI was lower in *Ban* (29±4 *vs.* 32±7 in *Be*; $p<0.02$), as were body fat (33±12 *vs.* 37±11 kg; *NS*) and waist diameter (99±9 *vs.* 106±16 cm; $p<0.02$). Forty-eight and 72% of *Ban* and *Be* were on metformin ($p<0.05$), while insulin was given to 39 and 34%. Daily insulin dose was lower in *Ban* (0.31±0.20 *vs.* 0.47±0.18 $IU.kg^{-1}.24h^{-1}$; $p<0.001$).

There was no difference in ß-cell function (%ß; *normal : 100%*) or insulin sensitivity (%S; *normal :100%*) as determined with HOMA between groups. %ß (median [perc 25-75]) was 51 [23-119] and 67 [45-84] in *Ban* and *Be*, while %S was 32 [29-37] and 37 [27-45]. Smoking (past & current) prevalence was 5 and 47% in *Ban* and *Be* ($p<0.0001$). Prevalence of micro- and macroangiopathy did not differ between groups, although *Ban* had more macroalbuminuria (29 *vs.* 9 %; $p<0.05$), and were more often treated with Ca^{2+}-channel- and ß-blockers than *Be* subjects (36 and 39 % *vs.* 16 and 8 %; p= 0.07 and <0.05, respectively).

Fasting (F) and interprandial (IP) triglycerides (TG) were lower in *Ban* : 115 [81-149] *vs.* 189 [155-325] $mg.dL^{-1}$ for F-TG and 127 [81-160] *vs.* 170 [128-305] $mg.dL^{-1}$ for IP-TG ($p<0.0001$), as was total cholesterol (201±53 *vs.* 223±40 $mg.dL^{-1}$ ($p<0.05$), despite lower use of hypolipidaemic drug (13 *vs.* 44%; $p<0.01$). African-heritage subjects with type 2 diabetes have similar degree of diabetes control and complications, in the presence of leaner biophysical status, minimal tobacco exposure and lower fasting and interprandial triglycerides.

Service d'Endocrinologie et Nutrition,
Cliniques Universitaires St Luc, UCL-DIAB 54.74,
Avenue Hippocrate 54, B-1200 BRUSSELS (Belgium)

Address for Correspondence :
Prof Dr Michel P. HERMANS,
Service d'Endocrinologie et Nutrition,
Cliniques Universitaires St Luc, UCL-DIAB 54.74,
Avenue Hippocrate 54, B-1200 BRUSSELS (Belgium)
Fax : +32 2 764.54.18

INTRODUCTION

Type 2 diabetes mellitus is a common condition arising from varying degrees of abnormalities in ß-cell secretion, insulin sensitivity and glucose effectiveness. It is considered to result from a combination of genetic predisposition and environmental-lifestyle factors associated with visceral adiposity and the development of insulin resistance, in susceptible individuals with defective ß-cell function unable to respond in the long-term with increased insulin secretion (1, 2).

The prevalence of type 2 diabetes exhibits worldwide differences according to ethno-geographic origin (3-10), rural-urban population distribution, and environmental factors mostly related to lifestyle (e.a. physical inactivity and dietary fat intake) leading to, or associated with, obesity and/or android body fat distribution (11-20). As a result from increased migration from sub-Saharan Africa and/or high diabetes prevalence, Bantu subjects represent nowadays the second largest non-EEC group attending our *Diabetes Clinic*.

The aim of the present study was to compare the clinical, biophysical and biochemical profiles (including diabetes history, age at diagnosis, medication use, degree of impairment in ß-cell function and insulin resistance, and prevalence of micro- and macroangiopathic complications) in two cohorts of outpatient subjects with type 2 diabetes, one from Bantu and the other from Belgian extraction, both followed at St Luc Hospital.

SUBJECTS AND METHODS

We evaluated 337 consecutive patients with type 2 diabetes from Belgian (*n*=314) or Bantu extraction (*n*=23) regularly followed at our Diabetes Clinic. These two cohorts were compared, and, due to significant differences in age between them, an age- and sex-matched sub-cohort of Belgian subjects (*n*=64) was further compared with the Bantu cohort.

Definition of diabetes was based on the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (21). Random venous plasma glucose was measured by a glucose oxidase method and HbA_{1c} by ion-exchange high performance liquid chromatography. The reported HbA_{1c} level is the median of values (*n*=2-4) obtained over the previous year. Lipid profile included total and LDL-cholesterol, HDL-cholesterol and triglycerides, which were measured using conventional methods. Total body fat was estimated by bioelectrical impedance analysis of body composition (*Bodyfat Analyser TBF-305*, Tanita Corporation, Japan).

The Homeostatic Model Assessment (HOMA) of insulin sensitivity and ß-cell function is based on the HOMA-CIGMA structural model of glucose/insulin interactions. It describes the metabolic responses of major effector organs, and allows for evaluating specific combinations of deficient ß-cell function and impaired insulin sensitivity provided by basal glucose and insulin concentrations. This model is validated against independent insulin sensitivity and ß-cell function indices, including clamp-derived measures (1, 22-25). For HOMA modelling, an antecubital cannula was inserted in the sampled arm, which was wrapped up in electrical blankets to provide « arterialised » blood, and three fasting samples were taken at 5 min intervals immediately after insertion of the cannula for RIA insulin and glucose assays used for modelling. After completion of each test, subjects were provided with a light meal.

The presence of peripheral neuropathy was based on clinical examination (knee and ankle reflexes, Semmes-Weinstein monofilament) and/or electromyography. The diagnosis of retinopathy was established on the basis of an eye visual examination by an experienced ophtalmologist and/or by fluorescein angiography. The presence of microalbuminuria was assessed by immunonephelometry (BN II, Behring, USA) and defined as urinary albumin concentration greater than 20 mg/l and less than 200 mg/l on a random sample or as excretion between 30 and 300 mg/24h. Creatinine clearance levels ($ml.min^{-1}$) were estimated using Gault & Cockroft's formula.

Hypertension was considered in all patients treated with antihypertensive drugs and/or in subjects previously diagnosed with hypertension according to systolic blood pressure >140 and/or diastolic blood pressure >90 mm/Hg. Macroangiopathy was considered in patients who had a history of cardiovascular event and/or in the presence of angina, claudication, abolished peripheral pulses and/or permanent ischemic electrocardiogram abnormalities at rest, or ischemic abnormalities in a stress test (usually combined with cardiac non-invasive imaging techniques).

STATISTICAL METHODS

Results are presented as means (± 1 SD) or as median [percentile 25 - percentile 75]. The significance of differences between means was assessed by Student's *t* test or by alternate Welch's *t* test for data sets with non-Gaussian distribution, and by Fisher's *Exact* test for differences in proportions. Results were considered significant or non-significant (NS) for $p <$ or ≥ 0.05 respectively.

RESULTS

Patients' characteristics are given in Tables 1 and 2. Bantu subjects were younger than the overall Belgian cohort (52±10 *vs*. 66±11 years; p<0.0001), and had a more masculine sex ratio (*NS*). Age at diabetes diagnosis and (known) diabetes duration were significantly higher in Belgian subjects, as was daily insulin dose. Waist circumference was also higher in Belgian subjects, but the difference was only marginally significant (103±14 *vs*. 99±9 cm; p=0.06; Table 1). Achieved education levels, HbA_{1c}, and proportions of subjects treated with metformin, sulfonylurea and/or insulin were not different between groups. Past/present smoking prevalence was much higher in Belgian than in Bantu subjects (49 *vs*. 5%; p<0.0001).

Due to the significant difference in age, an age- and sex-matched sub-cohort of Belgian subjects (n=64) was subsequently compared with the Bantu cohort. Diabetes duration and age at diabetes diagnosis were no longer significantly different between the two ethnic groups, whereas there were significant differences in smoking prevalence, BMI, waist circumference, metformin use and daily insulin dose, all of which were significantly lower in Bantu subjects (Table 1). Absolute fat mass was higher (+ 4 kg) in the Belgian sub-cohort, although the difference did not reach statistical significance (37 ± 11 *vs*. 33 ± 12 kg; *NS*).

There was no statistical difference between the overall Belgian (n=314) and Bantu cohorts with regards to systolic or diastolic blood pressure (BP), hypertension prevalence, BP lowering classes' usage, nor to the presence of retinopathy and peripheral neuropathy. Macroangiopathy prevalence was higher, though not significantly, in Belgian subjects (39 *vs*. 22%). Peripheral and coronary artery disease (PAD and CAD) prevalence was higher in Belgian subjects (16 (PAD) and 27% (CAD) *vs*. 4 (PAD) and 13% (CAD) in Bantu subjects, *NS*). Prevalence of transient ischemic attack &/or stroke was 7 (Belgian) and 4% (Bantu), respectively (*NS*).

Table 1 : Patients characteristics (1)

		Belgian	Belgian Subgroup	Bantu	p_1	p_2
n		314	64	23		
age	yr	66 (11)	52 (7)	52 (10)	*<0.0001*	–
M / F	%	59/41	61/39	61/39	*NS*	–
smoking (N-Ex-Y)*	%	51-36-13	53-26-21	95-5-0	*<0.0001***	*<0.001***
education (1-2-3-4)	%	37-23-27-13	42-12-34-12	37-19-19-25	*NS****	*NS****
age at diabetes diagnosis	yr	51 (11)	42 (8)	43 (7)	*<0.001*	*NS*
diabetes duration	yr	14 (9)	11 (8)	9 (9)	*<0.02*	*NS*
BMI	$kg.m^{-2}$	30.1 (6.0)	32.2 (7.4)	29.1 (3.7)	*NS*	*<0.02*
waist circumference	cm	103 (14)	106 (16)	99 (9)	*NS*	*<0.02*
fat mass	kg	33 (11)	37 (11)	33 (12)	*NS*	*NS*
HbA_{1c}	%	8.3 (1.6)	8.5 (1.9)	8.1 (1.9)	*NS*	*NS*
metformin	%	45	72	48	*NS*	*<0.05*
sulfonylurea	%	52	57	43	*NS*	*NS*
insulinotherapy	%	48	34	39	*NS*	*NS*
Daily insulin	$U.kg^{-1}.d^{-1}$	0.49 (0.33)	0.47 (0.18)	0.31 (0.20)	*<0.001*	*<0.001*

Means (1SD); * : N / Ex / Y = never / former / current smokers; p_1 : significancy of differences between Belgian (n=314) and Bantu subjects; p_2 : significancy of differences between age- and sex-matched Belgian Subgroup (n=64) and Bantu subjects; ** : non- *vs*. (former + current smokers); *** : (1 + 2) *vs*. (3 + 4).

Table 2 : Patients characteristics (2)

		Belgian	Belgian Subgroup	Bantu	p_1	p_2
n		314	64	23		
systolic BP	mm Hg	153 (23)	145 (21)	150 (23)	*NS*	*NS*
diastolic BP	mm Hg	86 (13)	88 (13)	88 (11)	*NS*	*NS*
HBP	%	67	62	65	*NS*	*NS*
n BP lowering drug(s)*	%	47-30-19-4	61-18-14-7	21-36-29-14	*<0.05*#	*<0.005*#
ACE-I & AIIA	%	46	44	43	*NS*	*NS*
beta-blockers	%	23	8	39	*NS*	*<0.005*
CCB	%	24	16	36	*NS*	*NS*
diuretic	%	22	14	22	*NS*	*NS*
lipid lowering drugs	%	34	44	13	*<0.05*	*<0.02*
retinopathy	%	34	30	29	*NS*	*NS*
polyneuropathy	%	50	38	25	*<0.05*	*NS*
glomerular filtration rate	$ml.min^{-1}$	80 (32)	112 (34)	87 (28)	*NS*	*<0.005*
normoalbuminuria	%	64	80	71	*NS*	*NS*
microalbuminuria	%	22	11	0	*<0.01*	*NS*
macroalbuminuria	%	14	9	29	*NS*	*<0.05*
macroangiopathy	%	39	18	22	*NS*	*NS*
PAD	%	16	9	4	*NS*	*NS*
CAD	%	27	12	13	*NS*	*NS*
TIA/stroke	%	7	2	4	*NS*	*NS*

Means (1SD); p_1 : significancy of differences between Belgian (*n*=314) and Bantu subjects; p_2 : significancy of differences between age- and sex-matched Belgian Subgroup (n=64) and Bantu subjects; * : expressed as % of hypertensive subjects treated with *n* = 1, 2, 3 or 4 BP-lowering drug(s); ACE-I : angiotensin-converting-enzyme inhibitor; AIIA : angiotensin-II-receptor antagonist; BP : blood pressure; CCB : calcium channel blocker; HBP : high blood pressure; # : mono- *vs*. poly-therapy; PAD : peripheral artery disease; CAD : coronary artery disease; TIA : transient ischemic attack.

Estimated glomerular filtration rate and proportion of subjects with normoalbuminuria were not different between groups (Table 2). On the other hand, there were significant differences in the proportion of subjects using a BP lowering drug monotherapy *vs*. those on polytherapy (47 *vs*. 21% in Belgian and Bantu respectively; $p<0.03$), as well as in lipid lowering drug usage (34 *vs*. 13% in Belgian and Bantu; $p<0.04$). There were also significant differences in peripheral neuropathy, as well as in the ratio of micro- to macro-albuminuric subjects (Table 2).

When the age- and sex-matched subgroup of Belgian subjects was compared with the Bantu cohort for the same parameters, the difference in peripheral neuropathy and microalbuminuria prevalences was no longer significant, whereas other differences became apparent with regards to higher use of ß-blockers and CCBs in Bantu subjects ($p<0.005$ for ß-blockers; $p=0.07$ for CCBs). Glomerular filtration rate was markedly lower in Bantu subjects (87 ±28 *vs*. 112 ± 34 $ml.min^{-1}$; $p<0.005$), who were more often in the macroproteinuric stage (29 *vs*. 9% ; Table 2).

Subjects' metabolic characteristics are shown in Table 3. There was no difference between the overall Belgian and Bantu cohorts with regards to fasting cholesterol (C), LDL-C, HDL-C, $C.HDL-C^{-1}$, and ß-cell function as modelled with HOMA. On the other hand, there were significant differences in fasting and interprandial triglycerides (TG), which were markedly higher in Belgian subjects ($p<0.01$ and 0.0001 respectively), as well as in uric acid and in fibrinogen (respectively higher and lower in Bantu subjects; $p<0.01$ and 0.05). Modelled insulin sensitivity (HOMA %S) was also significantly lower in Bantu subjects than in the overall Bel-

Table 3 : Metabolic Parameters

		Belgian	Belgian Subgroup	Bantu	p_1	p_2
n		314	64	23		
cholesterol (C)	$mg.dL^{-1}$	214 (43)	223 (40)	201 (53)	*NS*	*<0.05*
LDL-C	$mg.dL^{-1}$	128 (36)	131 (36)	128 (53)	*NS*	*NS*
HDL-C	$mg.dL^{-1}$	46 (15)	43 (14)	46 (18)	*NS*	*NS*
C/HDL-C		5.1 (1.9)	5.5 (1.6)	4.8 (1.9)	*NS*	*NS*
fasting TG	$mg.dL^{-1}$	163 [107-241]	189 [155-325]	115 [81-149]	*<0.005*	*<0.0001*
interprandial TG	$mg.dL^{-1}$	179 [130-280]	170 [128-305]	127 [81-160]	*<0.0001*	*<0.0001*
uric acid	$mg.dL^{-1}$	5.5 (1.6)	5.4 (1.5)	6.8 (2.3)	*<0.02*	*<0.02*
fibrinogen	$mg.dL^{-1}$	386 (111)	364 (108)	339 (104)	*<0.05*	*NS*
% S HOMA	%	41 [32-52]	37 [27-45]	32 [29-37]	*<0.0005*	*NS*
% B HOMA	%	55 [34-79]	67 [45-84]	51 [23-119]	*NS*	*NS*

Means (1SD) or means [interquartile rage]; p_1 : significancy of differences between Belgian (*n*=314) and Bantu subjects; p_2 : significancy of differences between age- and sex-matched Belgian Subgroup (*n*=64) and Bantu subjects; TG : triglycerides.

gian cohort ($p<0.05$; Table 3). There were negative relationships between BMI or waist diameter and HOMA %S in *Be* subjects (R^2 : 0.21 and 0.23 respectively) and between waist diameter and HOMA %S in *Ban* subjects (R^2 : 0.16), although there was no relationship between BMI and HOMA %S in the latter (R^2 : 0.001) (*not shown*).

When the age- and sex-matched subgroup of Belgian subjects was compared with the Bantu cohort for these metabolic parameters, differences in fibrinogen level and insulin sensitivity were no longer significant. Fasting and interprandial TG remained markedly lower in Bantu subjects, while fasting C was also found lower by ≈10% in Bantu subjects (201 ± 53 *vs*. 223 ± 40 $mg.dl^{-1}$; $p<0.05$; Table 3).

DISCUSSION

Bantu subjects represent 6.0% of all subjects regularly attending our *Diabetes Clinic*, thus ranking as the 4th largest attending group based upon ethno-geographical extraction, superseded by Belgian subjects (73.0%) and by subjects from Maghreb (8%) and Italian (6%) extractions respectively (*data not shown*). Our comparative study shows that Bantu subjects were markedly younger, had their diabetes diagnosed at a much earlier age, and had a significantly shorter known duration of diabetes than a general cross-sectional control group of consecutive Belgian subjects. This is in accordance with the well-recognised observation that Bantu subjects often present at the time of diagnosis with clinical features reminiscent of type 1 diabetes, while subsequently following a clinical course more compatible with type 2 diabetes (26). Diabetes in Africans is predominantly of the type 2 form, and Type 1 diabetes was excluded from our analysis on clinical & biochemical grounds (including lack of residual C-peptide &/or absence of (in)direct auto-immune markers). Yet, the presentation of type 2 diabetic subjects at diagnosis can often be misleading, as reviewed by Sobngwi *et al*. (40)

In order to better analyse differences between groups more directly relevant to interpret any effect of the ethno-geographical background, we subsequently compared this Bantu cohort with an age- and sex-matched Belgian cohort. Such a comparison provided with two groups of similar (known) diabetes duration and age at diabetes diagnosis, and, allegedly, similar exposure to hyperglycaemia. Both groups showed a globally similar overall glycaemic control, although Bantu subjects had lower HbA_{1c} (-0.4 %). Both groups exhibited similar prevalence of micro- and macro-angiopathy, although

Bantu subjects had a higher prevalence of macroalbuminuria and showed lower GFR figures.

On the other hand, Bantu subjects exhibited a markedly lesser prevalence of smoking and a higher usage of BP lowering drugs (especially ß- and CCBs), the latter being prescribed more often as polytherapy than in Belgian subjects. With regards to lipids, fasting- and interprandial triglycerides as well as total cholesterol were lower in Bantu subjects despite lesser usage of hypolipidemic drugs.

Risk factors for type 2 diabetes (essentially obesity, sedentarity, high fat intake, and familial predisposition) are not different in African or Caucasian subjects, although their prevalence is thought to be increased in African-Americans, due e.a. to differences in socio-economic status, increase incidence of obesity, and/or other genetic factors leading to diabetes-prone phenotypes (27).

Both in Caucasian and Bantu subjects, there is an inverse relationship between insulin sensitivity and abdominal fat (28). In our study, Bantu subjects showed a lesser degree of central adiposity compared with the age- and sex-matched Belgian cohort, together with a (non-significant) lesser amount of total body fat. They also showed HOMA-derived insulin sensitivity and ß-cell function indices similar to those of the age- and sex-matched controls, in the wake of similar (known) diabetes duration. This indirectly suggests that, for a given (abdominal) fat mass, Bantu subjects are relatively more insulin resistant than their Belgian counterparts.

There is some degree of controversy as to whether subjects from African ancestry having adopted a westernised life-style, either *in situ* or following (recent or ancient) migration, are more insulin-resistant than white Caucasians. Using oral glucose tolerance tests and Minimal Model analysis of insulin sensitivity and glucose-dependent glucose disposal, Osei *et al*. showed that Black Americans of African ancestry with normal glucose tolerance have lower basal and post-prandial hepatic extraction of insulin together with decreased insulin sensitivity and a trend toward decreased glucose effectiveness, when compared to white Caucasians subjects (29, 30). Studies of Ghanaian immigrants having recently migrated to the Western world performed by the same authors showed how rapidly such metabolic changes do indeed occur (31).

In the I.R.A.S. study, a survey of insulin sensitivity and cardiovascular risk in various ethnic minorities in the USA, Haffner et al. reported that the proportion of insulin-sensitive subjects was equally low in all groups (African-Americans, Hispanics and non-Hispanic whites), and that insulin resistance characterised all groups (32). On the other hand, Banerji and Lebovitz reported that most Black American subjects with normal weight had normal insulin sensitivity, while only 60% of subjects with BMI <30 kg.m^{-2} were insulin resistant (33). The UKPDS XII also assessed differences between Asians, Afro-Caribbeans and white Caucasians at diagnosis of diabetes, and found that Afro-Caribbean subjects had lower HOMA-derived ß-cell function and higher insulin sensitivity in the presence of lower triglycerides and higher HDL-cholesterol, with no difference in prevalence of micro- or macroangiopathic complications at diagnosis (20).

Our results also showed a similar degree of micro- and macroangiopathy in Bantu and in age- and sex-matched Belgian subjects when analysed cross-sectionally after a mean 10 years of *known* diabetes duration. This might at first sight seem odd since there were marked differences in conventional CV risk factors. The Atherosclerosis Risk In Communities (ARIC) study showed that diabetes conveys a high risk of coronary artery disease in Black subjects (34). In our study, Bantu subjects had significantly lower fasting- and inter-prandial triglycerides and total cholesterol, and a non-significant trend toward higher HDL-cholesterol level, despite lower usage of hypolipidemic drugs.

Such lipid profile combined with markedly lesser exposure to tobacco smoke might theoretically contribute to decrease their risk for macroangiopathy. On the other hand, BP control was less than satisfactory in both groups according to revised JNC-VI figures for therapeutic intervention, especially in Bantu subjects, who often required multiple BP lowering therapy, suggesting innate resistance to BP lowering drugs. Hypertension prevalence is known to be markedly higher (up to 50%) in Bantu extraction subjects than in Caucasians (35-37). As expected from earlier studies, we also found a higher usage of ß-blockers and/or CCBs agent(s) for BP control in Bantu subjects (37).

Poorer BP control and (possibly) lesser insulin sensitivity could easily offset the benefits of better lipid profile and lesser tobacco smoke exposure. Thus, the

UKPDS studies highlighted the paramount importance of appropriate BP control for the development of micro- and macroangiopathy in type 2 diabetes, and the cluster of abnormalities associated with insulin resistance was recently shown to be independently associated with CV risk in type 2 diabetic subjects (38, 39).

We conclude that African-heritage subjects with type 2 diabetes have broadly similar levels of diabetes control and of macroangiopathic complications following a similar (known) duration of diabetes. This was observed in the presence of a leaner biophysical status, of minimal tobacco exposure, of lesser fasting and inter-prandial triglycerides, and of higher requirement for blood pressure lowering drugs. When compared with sex- and age-matched white Caucasian controls, they did not show significant differences in insulin sensitivity or ß-cell function when matched for similar diabetes duration.

AKNOWLEDGMENTS

This study was supported by the *European Association for the Study of Diabetes* (EASD) and by the *Association Belge du Diabète* (ABD).

REFERENCES

1. Rudenski AS, Hadden DR, Atkinson AB, Kennedy L, Matthews DR, Merret JD, Pockaj B, Turner RC. Natural history of pancreatic islet B-cell function in Type 2 diabetes mellitus studied over 6 years by Homeostasis Model Assessment. *Diabetic Med.* 1988; 5: 36-41.
2. Rudenski AS, Matthews DR, Levy JC, Turner RC. Understanding "Insulin Resistance" : both glucose resistance and insulin resistance are required to model human diabetes. *Metabolism.* 1991; 40: 908-17.
3. Carter JS, Pugh JA, Monterrosa A. Non-insulin-dependent diabetes mellitus in minorities in the United States. *Ann Intern Med.* 1996; 125: 221-32.
4. Fujimoto WY. Overview of non-insulin-dependent diabetes mellitus (NIDDM) in different population groups. *Diabet Med.* 1996; 13(Suppl 6), S7-S10.
5. Hara H, Egusa G et al. Incidence of non-insulin-dependent diabetes mellitus and its risk factors in Japanese-Americans living in Hawaii and Los Angeles. *Diabet Med.* 1996; 13(Suppl 6): S133-42.
6. King H, Rewers M. Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. WHO Ad Hoc Diabetes Reporting Group. *Diabetes Care.* 1993; 16: 157-77.
7. King H, Zimmet P et al. Ethnic differences in susceptibility to non-insulin-dependent diabetes. A comparative study of two urbanized Micronesian populations. *Diabetes.* 1984 ; 33: 1002-7.
8. Pereira MA, Kriska AM et al. Physical inactivity and glucose intolerance in the multiethnic island of Mauritius. *Med Sci Sports* Exerc. 1995; 27: 1626-34.
9. Ramachandran, A, Snehalatha C, Viswanathan V, Viswanathan M, Haffner SM. Risk of non-insulin dependent diabetes mellitus conferred by obesity and central adiposity in different ethnic groups : a comparative analysis between Asian Indians, Mexican Americans and Whites. *Diabetes Res Clin Pract.* 1997; 36 : 121-5.
10. Samanta A, Burden AC et al. Comparative prevalence of non-insulin-dependent diabetes mellitus in Asian and white Caucasian adults. *Diabetes Res Clin Pract.* 1987; 4: 1-6.
11. Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. *Annu Rev Med.* 1998; 49: 235-61.
12. Greenhalgh PM. Diabetes in British South Asians : nature, nurture, and culture. *Diabet Med.* 1997; 14: 10-8.
13. James S A, Jamjoum L et al. Physical activity and NIDDM in African-Americans. The Pitt County Study. *Diabetes Care.* 1998; 21: 555-62.
14. McKeigue PM, Shah B et al. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet.* 1991; 337: 382-6.
15. Ostbye T, Welby TJ et al. Type 2 (non-insulin-dependent) diabetes mellitus, migration and westernisation : the Tokelau Island Migrant Study. Diabetologia. 1989; 32: 585-90.
16. Potts J, Simmons D. Sex and ethnic group differences in fat distribution in young United Kingdom South Asians and Europids. *J Clin Epidemiol.* 1994 ; 47: 837-41.
17. Ramachandran A, Snehalatha C et al. Prevalence of glucose intolerance in Asian Indians. Urban-rural difference and significance of upper body adiposity. *Diabetes Care.* 1992; 15: 1348-55.
18. Ramachandran A, Snehalatha C et al. Risk of noninsulin dependent diabetes mellitus conferred by obesity and central adiposity in different ethnic groups : a comparative analysis between Asian Indians, Mexican Americans and Whites. *Diabetes Res Clin Pract.* 1997; 36: 121-5.
19. Stern MP. Kelly West Lecture. Primary prevention of type II diabetes mellitus. *Diabetes Care.* 1991; 14: 399-410.
20. UKPDS Group. UK Prospective Diabetes Study XII : Differences between Asian, Afro-Caribbean and white Caucasian type 2 diabetic patients at diagnosis of diabetes. *Diabet Med.* 1994; 11: 670-7.
21. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care.* 1997; 20: 1183-97.
22. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis Model Assessment : insulin resistance and ß-cell function from fasting plasma glucose and insulin concentration in man. Diabetologia. 1985; 28: 412-9.
23. Hermans MP, Levy JC, Morris RJ, Turner RC. Comparison of insulin sensitivity tests across a range of glucose tolerance from normal to diabetes. *Diabetologia.* 1999; 42: 678-87.
24. Hermans MP, Levy JC, Morris RJ, Turner RC. Comparison of tests of b-cell function across a range of glucose tolerance from normal to diabetes. *Diabetes.* 1999; 48 : 1779-86.
25. Levy JC, Matthews DR, Hermans MP. Correct Homeostasis Model Assessment (HOMA) evaluation uses the computer program. *Diabetes Care.* 1998; 21: 2191-2.
26. Gautier J-F, Sobngwi E, Vexiau P. Comment je traite et prends en charge un diabète du sujet noir. In : Journées Annuelles de Diabétologie de l'Hôtel-Dieu 2001, pp165-178, Flammarion Médecine-Sciences (Paris).

27. Haffner SM. Epidemiology of type 2 diabetes : risk factors. *Diabetes Care*. 1998; 21(Suppl 3): C3-6.
28. Banerji MA, Chaiken RL, Gordon D et al. Does intra-abdominal adipose tissue in black men determine whether NIDDM is insulin-resistant or insulin-sensitive? *Diabetes*. 1995; 44: 141-6.
29. Osei K, Cottrell DA. Minimal model analysis of insulin sensitivity and glucose-dependent glucose disposal in black and white Americans : a study of persons at risk for type 2 diabetes. *Eur J Clin Invest*. 1994; 24: 843-50.
30. Osei K, Schuster DP. Ethnic differences in secretion, sensitivity, and hepatic extraction of insulin in Black and White Americans. *Diabet Med*. 1994; 11: 755-62.
31. Osei K, Schuster DP. Metabolic characteristics of African descendants : a comparative study of African-American and Ghanaian immigrants using minimal model analysis. *Diabetologia*. 1995; 38: 1103-9.
32. Haffner SM, Howard G, Mayer E, Bergman RN, Savage PJ, Rewers M, Mykkänen L, Karter AJ, Hamman R, Saad MF. Insulin sensitivity and acute insulin response in African-Americans, non-Hispanic Whites, and Hispanics with NIDDM. The Insulin Resistance Atherosclerosis Study. *Diabetes*. 1997; 46: 63-9.
33. Banerji MA, Lebovitz HE. Insulin action in Black Americans with NIDDM. *Diabetes Care*. 1992; 15: 1295-302.
34. Folsom AR, Szklo M, Stevens J, Liao F, Smith R, Eckfeldt JH. A prospective study of coronary heart disease in relation to fasting insulin, glucose, and diabetes. The Atherosclerosis Risk in Communities (ARIC) Study. *Diabetes Care*. 1997; 20: 935-42.
35. Cooper R, Rotimi C. Hypertension in blacks. *Am J Hypertens*. 1997; 10: 804-12.
36. Ferrannini, E., S. M. Haffner, et al. High blood pressure and insulin resistance : influence of ethnic background. *Eur J Clin Invest*. 1991 ; 21: 280-7.
37. Jamerson K, DeQuattro V. The impact of ethnicity on response to antihypertensive therapy. *Am J Med*. 1996; 101(Suppl 3A): S22-32.
38. U.K. Prospective Diabetes Study (UKPDS 55). Davis TME, Cull CA, Holman RR for the U.K. Prospective Diabetes Study (UKPDS) Group. Relationship between ethnicity and glycaemic control, lipid profiles, and blood pressure during the first 9 years of type 2 diabetes. *Diabetes Care*. 2001; 24: 1167-74.
39. Haffner SM, Williams K, Rozek MM, Stern MP. Homeostasis Model Assessment of insulin resistance in relation to 8-years of incidence of cardiovascular diseases. *Diabetologia*. 2000; 43(Suppl 1): A282.
40. Sobngwi E, Mauvais-Jarvis F, Vexiau P, Mbanya JC, Gautier JF. Diabetes in Africans. Part 1 : epidemiology and clinical specificities. *Diabetes Metab* 2001; 27: 628-34.