

Original article

CHARACTERIZATION OF TYPE 2 DIABETES MELLITUS IN FIRST GENERATION ITALIAN MIGRANTS TO BELGIUM

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ABSTRACT

Type 2 diabetes mellitus is a major metabolic disease in developed countries, and preferentially affects low-income groups and/or people from Southern extraction. Migrants are especially at risk. In Belgium, a large population of workers emigrated in the 50s and 60s, especially from rural areas of Southern Italy and Sicily. We tested the hypothesis that type 2 diabetes mellitus' phenotype in these Italian migrants could differ from that observed in autochthonous Belgian subjects. We retrospectively compared the clinical files of 485 patients with type 2 diabetes either of Belgian (n=445) or Italian origin (n=40). Italians were younger at diagnosis (46±14 vs. 52±13 years, $P<0.01$), shorter, had a lower education and a stronger family record of diabetes (89 vs. 47%, $P<0.01$). They had similar BMIs (31±6) and similar or slightly worse degree of sedentarity (>75%). We further compared this Italian group to 115 Belgians subjects matched for age, sex, and education. Known duration of diabetes (16 years), smoking and drinking habits, use of oral hypoglycaemic, an-

tihypertensive and hypolipaeamic drugs, complications, CRP, estimated glomerular filtration rate, micro-albuminuria prevalence, blood pressure, insulin sensitivity/ beta-cell function estimated by HOMA modelling, as well as fat mass indirectly estimated by impedancemetry were not significantly different between the two populations. There was a non significant trend toward higher HbA1c (8.7± 2 vs. 8.2±2%, *NS*) in Italian subjects whose LDL-cholesterol was however significantly lower (105±31 vs. 120±33 mg.dL⁻¹, $P<0.01$) as well as folic acid (5±1.7 vs. 6.7±4, $P<0.001$). Insulin dose was higher (0.77±0.4 vs. 0.48±0.3 IU.day⁻¹, $P<0.001$) and abdominal obesity less prevalent in males (33 vs. 58%, $P<0.01$) of this group. Thus, Italian diabetic subjects in Belgium exhibit higher insulin requirements despite similar/better BMI, known duration of diabetes, HOMA indices, use of oral antidiabetic drugs, abdominal obesity and slightly higher HbA1c. This points towards different dietary habits, as do the differences in folic acid and LDL-cholesterol; different patterns of exercise may also play a role. Higher family record of diabetes may be genetic, but may also be biased by tighter family structure in subjects of Italian extraction.

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INTRODUCTION

Type 2 diabetes mellitus is a very common disorder whose increasing prevalence has been reported all over the world. Type 2 diabetes arises from different combinations of β -cell failure and insulin resistance, both promoted by genetic and environmental factors (1). In the past decades ethnicity was reckoned to be a major modifying factor affecting the natural history and presentation of Type 2 diabetes mellitus (2-6). Ethnicity is a broad concept that encompasses both genetic predispo-

sition and socio-cultural determinants of everyday life, including food choice, timing of food intake and exercise habits as well as body representation. Thus, it was convincingly demonstrated that the prevalence and presentation of Type 2 diabetes was different in Afro-Americans and Hispano-Americans by comparison to the traditional 'Caucasian' American patients (5). Belgium also shelters a multi-ethnic population, e.g. from the Maghreb and from sub-Saharan-Africa. We previously reported the phenotypic characteristics of African-heritage subjects with type 2 diabetes in this journal (7).

Another large population in Belgium is constituted by economic migrant workers of Italian extraction. They came to Belgium largely in the 50s and 60s, from the Southern part of the Italian Peninsula as well as from Sicily, mainly to work in coal mines in the Borinage, Centre and Liège areas. Due to the large number of concomitant migrants living in close-knit communities, most of the first generation maintained a relatively traditional way of life, including food selection and eating habits. Most of these first-generation migrant workers faced harsh economic conditions for years after their arrival in Belgium, which can predispose to the development of Type 2 diabetes (such as poor food choices, physical inactivity, weight gain, deleterious intrauterine environment, tobacco smoke and ethanol exposures).

So far, most epidemiological studies on Italian subjects were devoted to the peculiarities of Type 1 diabetic subjects originating mainly from Sicily and Sardinia(8). Oddly with respect to the presence of very large Italian migrant communities, especially in the USA, the characteristics of this population was never studied nor compared to native diabetic subjects. In Northern Italy, one study however showed that migrants from Southern Italy and Italian islands are characterized by a higher diabetes-linked mortality rate (9). We therefore analyzed the characteristics of Italian migrants with type 2 diabetic subjects, and compared them to a native Belgian population with the same condition, and to a matched sub-group for age, sex and education.

SUBJECTS AND METHODS

All medical records of type 2 diabetes subjects so far entered in our database ($n=485$) were analysed with respect to country of origin, in order to compare the characteristics of Belgian ($n=445$) vs. Italian ($n=40$) subjects. Preliminary comparison between these two

cohorts disclosed significant differences with regards to age and education (educational attainment was dichotomised within each group according to whether subjects had completed or not secondary or higher education). Due to the extent of differences, a sub-cohort of 115 Belgian patients matched for age, sex and education level, derived from the initial cohort, was incorporated for further comparison.

The Homeostatic Model Assessment (HOMA) model was used to appreciate insulin sensitivity and B-cell function. Total body fat was estimated by bi-brachial impedance analysis (Bodyfat Analyser BF-300). Other measurements were all by usual and commonly accepted methods (see ref 7 for further details). In both groups, homocysteine and folate measurements represent values prior to subsequent folate supplementation given to subjects with hyperhomocysteinaemia.

Results are presented as mean \pm SD or as proportion (%). The significance of differences between means was assessed by the *z* test for unmatched samples. The significance of differences between proportions was assessed by the *Fisher's exact test*. Results were considered non significant (NS) for $P > 0.05$.

RESULTS

Italian patients (Tables 1 and 2) were characterized by earlier age at diagnosis of diabetes (no longer present after matching), stronger family record of diabetes, stronger prevalence of current smoking, lower education level, a trend towards lower exercising, a shorter stature, lower prevalence of excess waist circumference (in males), as well as a non-significant trend towards higher HbA1c.

The use of antidiabetic, antihypertensive, hypolipidaemic and other commonly prescribed drugs was similar in the two groups. There were however markedly higher insulin requirements in subjects of Italian-heritage (Table 3). Blood pressure control was slightly better in Italian patients (Table 4) but without significant differences in various kidney indices (serum creatinine, estimated glomerular filtration rate, and (micro)albuminuria).

Lipid control was clearly better regarding LDL-cholesterol; by contrast, HDL-cholesterol was lower and triglycerides tended to be higher in Italian subjects. There were no significant differences in CRP, fibrinogen, uric acid and B12 vitamin. Folic acid and homocysteine were lower in Italian subjects (Table 5).

Table 1. Patients' characteristics (1) : socio-demographic

		Belgians	Belgian subgroup	Italians	P1	P2
<i>n</i>		445	115	40	~	~
age	years	68.8 (10.6)	63.5 (10.0)	63.2 (11.8)	<i>p</i> <0.01	~
age at diabetes diagnosis	years	51.8 (12.6)	48.2 (13.4)	46.3 (14.5)	<i>p</i> <0.01	NS
family history : diabetes	%	47	48	89	<i>p</i> <0.01	<i>p</i> <0.01
sex ratio (M/F)	%	62 : 38	62 : 38	62 : 39	~	~
smoking						
former	%	38	35	27	NS	NS
current	%	15	17	33	<i>p</i> <0.01	NS
tobacco smoke exposure	packs.year ¹	38 (27)	33 (31)	34 (19)	NS	NS
ethanol	U.week ⁻¹	16 (22)	12 (20)	11 (11)	NS	NS
education [§]	%	58 : 42	77 : 23	77 : 23	<i>p</i> <0.02	~
AMBG	%	80	79	86	NS	NS
exercise level						
none (sedentary)	%	79	75	89	NS	NS
light (walking, gardening)	%	17	20	5	NS	<i>p</i> <0.05
sport practice	%	4	6	5	NS	~

Results are expressed as means (1 SD) or as proportions (%). Differences between respective means were assessed by z test for unmatched samples between Italians (n=40) and Belgian (n=445) subjects (P1), or between Italians (n=40) and Belgians subjects matched for age, sex and education level (n=115 (Belgian subgroup); P2). Differences between respective proportions were assessed by Chi2or Fisher's exact test. Differences between column means or proportions were considered statistically significant at P values <0.05. NS: non significant; M: male; F: female; AMBG: ambulatory monitoring of blood glucose; §: lower- vs. higher education level.

Table 2. Patients' characteristics (2) : metabolic

		Belgians	Belgian subgroup	Italians	P1	P2
<i>n</i>		445	115	40	~	~
weight	kg	85.4 (17.3)	87.4 (15.7)	82.7 (15.9)	NS	NS
height	m	1.69 (0.09)	1.69 (0.08)	1.64 (0.09)	<i>p</i> <0.001	<i>p</i> <0.001
BMI	kg.m ⁻²	30.0 (5.6)	30.9 (5.9)	31.0 (5.8)	NS	NS
waist circumference	cm	104 (13)	106 (11)	105 (13)	NS	NS
> 102 cm (M)	%	40	58	33	NS	<i>p</i> <0.01
> 88 cm (F)	%	47	55	53	NS	NS
hip circumference	cm	107 (12)	108 (11)	105 (12)	NS	NS
fat mass (relative) [§]	%	33.3 (7.9)	33.7 (7.2)	34.8 (7.9)	NS	NS
fat mass (absolute) [§]	kg	28.4 (10.0)	28.8 (8.2)	29.4 (10.8)	NS	NS
HOMA S	%	47 (23.9741794549)	47 (26.5918090429)	44 (26)	NS	NS
HOMA B	%	60 (43.2019980419)	64 (46.5216283492)	60 (43)	NS	NS
diabetes duration	years	16.7 (10.9)	15.6 (12.2)	18.1 (9.9)	NS	NS
duration prior to insulin	years	11.7 (10.0)	11.4 (12.2)	10.9 (9.6)	NS	NS
HbA _{1c}	%	8.1 (1.6)	8.2 (1.7)	8.7 (2.0)	NS	NS
< 7.0 %	%	25	24	14	NS	NS

Results are expressed as means (1 SD) or as proportions (%). Differences between respective means were assessed by z test for unmatched samples between Italians (n=40) and Belgian (n=445) subjects (P1), or between Italians (n=40) and Belgians subjects matched for age, sex and education level (n=115 (Belgian subgroup); P2). Differences between respective proportions were assessed by Chi2or Fisher's exact test. Differences between column means or proportions were considered statistically significant at P values <0.05. NS: non significant; BMI: body mass (Quetelet's) index; M: males; F: females; HOMA S and HOMA B: insulin sensitivity and beta-cell function (normal values = 100 %) measured by the Homeostatic Model Assessment (computer-based) method. §: indirect bi-brachial bioimpedance measurement (OMRON BF 300).

Table 3. Pharmacologic agents

		Belgians	Belgian subgroup	Italians	P1	P2
<i>n</i>		445	115	40	~	~
beta-cell stimulant	%	48	50	39	NS	NS
metformin	%	50	59	63	NS	NS
insulin	%	53	56	63	NS	NS
insulin dose (absolute)	IU.day ⁻¹	44 (31)	43 (32)	64 (35)	<i>p</i> <0.01	<i>p</i> <0.05
insulin dose (relative)	IU.day ⁻¹ .kg ⁻¹	0.53 (0.34)	0.48 (0.29)	0.77 (0.44)	<i>p</i> <0.01	<i>p</i> <0.01
ACE-I	%	44	44	52	NS	NS
AIIA	%	11	15	10	NS	NS
CCB	%	26	24	21	NS	NS
beta-blocker	%	26	23	25	NS	NS
diuretic	%	27	27	31	NS	NS
low-dose ASA	%	41	34	37	NS	NS
nitrate	%	13	11	18	NS	NS
benzodiazepine(s)	%	27	31	29	NS	NS
anti-depressant(s)	%	19	15	21	NS	NS
statin	%	17	18	19	NS	NS
fibrate	%	23	26	19	NS	NS
HRT	%	31	23	23	NS	~
folate	%	14	14	7	NS	NS
vitamin B ₁₂	%	10	8	7	NS	NS

Results are expressed as means (1 SD) or as proportions (%). Differences between respective means were assessed by z test or Welsh's test for unmatched samples between Italians (n=40) and Belgian (n=445) subjects (P1), or between Italians (n=40) and Belgians subjects matched for age, sex and education level (n=115 (Belgian subgroup); P2). Differences between respective proportions were assessed by Chi2 or Fisher's exact test. Differences between column means or proportions were considered statistically significant at P values <0.05. NS: non significant; ACE-I: angiotensin-converting enzyme inhibitor; AIIA: angiotensin II receptor antagonist; CCB: calcium-channel blocker; ASA: acetylsalicylic acid; HRT: post-menopausal hormone replacement therapy.

Table 4. Blood pressure (BP) values, hypertension and kidney function

		Belgians	Belgian subgroup	Italians	P1	P2
<i>n</i>		445	115	40	~	~
Systolic BP (SBP)	mm Hg	148 (22)	144 (18)	139 (19)	<i>p</i> <0.05	NS
Diastolic BP (DBP)	mm Hg	82 (13)	81 (11)	79 (13)	NS	NS
Heart rate	b.p.m.	77 (13)	78 (14)	77 (14)	NS	NS
High blood pressure (HBP) prevalence	%	86	85	70	<i>p</i> <0.01	NS
Anti-hypertensive agent(s) use	%	72	70	78	NS	NS
Mono-, bi-, tri- and tetra/pentatherapy(ies)	%	43 - 29 - 18 - 10	38 - 36 - 17 - 9	40 - 36 - 16 - 8	NS	NS
creatinine	mg.dl ⁻¹	1.1 (0.5)	1.1 (0.6)	1.2 (0.9)	NS	NS
estimated GFR	ml.min ⁻¹	82 (34)	89 (33)	80 (37)	NS	NS
albuminuria	mg.l ⁻¹	32 (47)	27 (39)	42 (53)	NS	NS
microalbuminuria	%	31	25	32	NS	NS
clinical albuminuria	%	9	10	20	NS	NS

Results are expressed as means (1 SD) or as proportions (%). Differences between respective means were assessed by z test or Welsh's test for unmatched samples between Italians (n=40) and Belgian (n=445) subjects (P1), or between Italians (n=40) and Belgians subjects matched for age, sex and education level (n=115 (Belgian subgroup); P2). Differences between respective proportions were assessed by Chi2 or Fisher's exact test. Differences between column means or proportions were considered statistically significant at P values <0.05. NS: non significant; GFR: glomerular filtration rate (Cockcroft-Gault estimate).

Table 5. Laboratory values

		Belgians	Belgian subgroup	Italians	P1	P2
<i>n</i>		445	115	40	~	~
cholesterol	mg.dl ⁻¹	204 (40)	204 (38)	192 (61)	NS	NS
LDL-cholesterol	mg.dl ⁻¹	122 (34)	120 (33)	105 (31)	<i>p</i> <0.01	<i>p</i> <0.01
HDL-cholesterol	mg.dl ⁻¹	48 (14)	47 (15)	40 (10)	<i>p</i> <0.001	<i>p</i> <0.05
cholesterol:HDL ⁻¹		4.6 (1.6)	4.8 (1.8)	5.1 (2.1)	NS	NS
triglycerides (fasting)	mg.dl ⁻¹	183 (132)	209 (179)	252 (156)	<i>p</i> <0.01	NS
C-reactive protein (CRP)	mg.dl ⁻¹	0.5 (0.6)	0.5 (0.4)	0.5 (0.4)	NS	NS
fibrinogen	mg.dl ⁻¹	374 (100)	346 (78)	374 (135)	NS	NS
uric acid	mg.dl ⁻¹	5.6 (1.7)	5.6 (1.6)	6.1 (2.2)	NS	NS
homocysteine (plasma)	μmol.l ⁻¹	15.2 (6.5)	14.7 (5.6)	12.5 (4.8)	<0.01	<0.02
> 15 μmol.l ⁻¹	%	44	42	28	NS	NS
folic acid (serum)	ng.ml ⁻¹	6.7 (4.0)	6.7 (4.1)	5.0 (1.7)	<i>p</i> <0.001	<i>p</i> <0.001
B ₁₂ vitamin (serum)	pg.ml ⁻¹	542 (414)	533 (421)	509 (283)	NS	NS

Results are expressed as means (1 SD) or as proportions (%). Differences between respective means were assessed by z test or Welsh's test for unmatched samples between Italians (n=40) and Belgian (n=445) subjects (P1), or between Italians (n=40) and Belgians subjects matched for age, sex and education level (n=115 (Belgian subgroup); P2). Differences between respective proportions were assessed by Chi2 or Fisher's exact test. Differences between column means or proportions were considered statistically significant at P values <0.05. NS: non significant.

There was no significant difference, neither any diverging trend, in the prevalence of retinopathy, peripheral/autonomous neuropathy, or any form of macroangiopathy (*not shown*).

DISCUSSION

Ethnicity is increasingly considered a major determinant of the presentation, evolution and prognosis of type 2 diabetes mellitus in contemporary multicultural societies, and should be considered when elaborating health policies dealing with different sub-communities (2-6). Ethnicity is a large concept that encompasses genetic, cultural and socio-economic factors. This concept was originally developed to deal with the specificities of cardiovascular diseases, namely hypertension, in the Afro-American community, then in the Hispano-American community, and is now regarded as applicable to any migrant communities and to a variety of conditions. This is especially true in metabolic diseases where the phenotype is sensitive to varying ways of life and socio-economic conditions. The medical conditions of such sub-communities differ both from those of the area of extraction and from those of the native population in the area of installation.

Such differences may be advantageous, ea. lower

exposure to infectious diseases more endemic in Southern areas. Unfortunately, with regard to metabolic disease, the changes are mostly unfavourable: migrants lose partly the relative protection of a traditional way of life and choice of foods, and they are - at least for the first generation - confined to low socio-economical roles often associated with increased metabolic risk mainly due to reduced food choice, increased smoking prevalence, and decreased caloric expenditure as a result of exercise and physical activities. Thus, when a country hosts a relatively large and close-knit community of migrants, it may be advantageous to study precisely the mode of presentation of largely prevalent diseases such as diabetes mellitus or hypertension. This may help develop more appropriate social and medical approaches towards these at-risk subjects.

In Belgium, Italian immigration was primarily economically-driven and took place mainly in the years fifties and sixties (10-12). People migrated largely from Southern Italy and Sicily to search work in the coal mining areas of Borinage, Centre and Liège. Until recently, these communities remain closely-knitted in these arrival areas.

Our work was not intended to document the prevalence of diabetes and cardiovascular diseases in migrants of Southern Italian extraction in Belgium. Subjective clinical feeling and common sense suggest

however that this prevalence is likely to be elevated. This was previously documented in economic migrants from Southern to more Northern Italy (9). In people originating from Southern Italy and Islands, ischaemic heart disease and diabetes mellitus-related mortalities were increased. This contrasted with cancer, AIDS or opioid-related mortalities (higher in people from Northern Italy). Increases in diabetes-related mortality were also pointed out in all studied minorities in the United States, to such an extent that they were ascribed to poor socio-economical conditions and education as well as to specific ethnic types (4).

Our data allowed us to compare the characteristics of type 2 diabetes mellitus observed in first generation migrants of Southern Italian extraction (now aged 60 or more) and in subjects of Belgian origin. Italian diabetic subjects were younger, younger at diabetes diagnosis, and had lower education status. This is not surprising considering the socio-economical conditions that dictated their move to migrate. We therefore compared them to a subgroup of Belgian subjects matched for age, sex and education level for further comparisons. The difference in age at diabetes diagnosis was no longer present once compared to the Belgian sub-cohort matched for age, sex and education, since elderly and/or higher education Italian subjects are under-represented in our sample of relatively recent economic migrants. Furthermore, caution should be exercised regarding the potential underestimation between actual and known diabetes duration. At the anthropometric level, Italian subjects were shorter. This may reflect a predominantly Sicilian genetic background, but also selection. Indeed, people were somehow medically selected before migration, with the intention to exclude people who were not deemed fit for the harsh work of mining. We do not know whether such selection included any criteria of height (favouring for instance shorter individuals).

The most striking information of this study was the significantly increased insulin requirements of Italian insulin-treated subjects. This was not due to anthropometric variables, as BMI, waist circumference, fat mass were all comparable in both groups. Neither was it due to longer diabetes' known duration nor to different diabetes time extents prior to initiating insulin therapy. Furthermore this was not related to lower insulin sensitivity or to premature decline of beta-cell function (as reflected by the HOMA-S and HOMA-B indexes). Italian subjects had a lower usage of beta-cell stimulating drug(s), which could partly account

for the difference in exogenous insulin requirements. Since such drug use difference was small and non-significant, the magnitude of this influence is unlikely to play a major role on insulin requirements. On the other hand, physical activity may partly explain the increased insulin requirements. Although poor in both populations, it was worse in Italian subjects when compared to matched Belgian subjects. Another possible explanation is different food choices. Up to now, most Italian migrants maintained relatively traditional Italian food selection, favouring vegetables, pasta, olive oil and less meat, especially pork, and butter that are both very liberally consumed by Belgian subjects. It is demonstrated that some aspects of the traditional Mediterranean-diet have a beneficial influence on blood glucose response(13), with certain pastas comparing favourably with white bread or potato dumplings that are more traditional Belgian sources of carbohydrates. On the other hand, it is not demonstrated that migrants to Northern latitudes do indeed maintain all beneficial components of the Mediterranean-diet, both quantitatively and qualitatively. An indication favouring the conflicting influence of hygienic-dietetic behaviours and food choices may also be inferred from the dual observation of significantly lower LDL-cholesterol and HDL levels in Italian subjects, especially since ethanol intake and HRT use, two potential confounding factors, were not different from those of age-, sex- and education-matched Belgians.

The present study points towards dietary and physical activity determinants at play in the diabetes phenotype of Italian migrants. This is in striking difference with another large group of economic migrants living in Belgium, namely African-heritage subjects with type 2 diabetes living in Belgium(7). These were mainly characterized by leaner morphometrics, less tobacco exposure and lower plasma triglycerides, and were treated by different antihypertensive drug regimens compared with matched Belgian subjects.

Finally, Italian subjects mentioned a higher prevalence of family history for diabetes mellitus. It is difficult to determine whether this really reflects a higher genetic susceptibility to diabetes or a tighter familial structure allowing more efficient recording and updating of diabetes incidence and prevalence. It could also be due to the fact that emigration often was chosen by several members of the same family, who were thus similarly exposed to the socio-economical determinants of the expression of type 2 diabetes mellitus.

CONCLUSIONS

We compared the current characteristics of Type 2 diabetic subjects either of Belgian or Italian origin. Compared with unmatched Belgians, Italians were younger at diagnosis, had a lower education index. To correct for these parameters we included in the comparison a matched cohort of Belgian subjects. Insulin requirements of Italian subjects were markedly higher despite similar morphometrics. This could be in part explained by a lower level of physical activity, lesser use of beta-cell stimulants, and/or different food selections. A higher familial history of diabetes in Italian subjects may be truly genetic, or due to shared migratory pattern within the family, or else be an artefact explained by tighter familial structure in Italian communities.

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