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A family history of diabetes determines poorer glycaemic control and younger age of diabetes onset in immigrants from the Middle East compared with native Swedes

Glycaemic control in Iraqi immigrants

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Abstract

Aims: Immigrant populations from the Middle East develop diabetes earlier than European indigenous populations; however, the underlying aetiology is poorly understood. The aims were to study risk factors associated with early diabetes onset and, in non-diabetics, to study glycaemic control in immigrants from Iraq and native Swedes.

Methods: This cross-sectional population-based study comprised 1,398 Iraqi immigrants and 757 Swedes (age 30-75 years) residing in the same area of Malmö, Sweden. Outcomes were age at diabetes onset and glycaemic control (HbA1c) assessed by Cox proportional hazards and linear regression respectively.

Results: In Iraqis versus Swedes, clustering of family history (family history in ≥2 relatives) was more prevalent (23.2 vs. 3.6%, $p<0.001$) and diabetes onset occurred earlier (47.6 vs. 53.4 years, $P=0.001$). Iraqi background independently raised the hazards for diabetes onset. Diabetes risk due to family history was augmented by obesity, with the highest hazard ratios observed in obese participants with clustering of family history (hazard ratio 5.1, 95% CI 3.2 to 8.2), after adjustment for country of birth and sex.

In participants without previously diagnosed diabetes (Iraqis N=1270; Swedes N=728), HbA1c levels were slightly higher in Iraqis than Swedes (4.5 vs. 4.4%, $P=0.038$). This difference was explained primarily by clustering of family history, rather than by age, obesity, lifestyle or socioeconomy.

Conclusions: This study shows that the greater predispotion to diabetes in Middle Eastern immigrants may be explained by more extensive family history of the disease; clinical interventions tailored to Middle Eastern immigrants with extensive family history are thus warranted.

Key words: heredity, hyperglycemia, Middle East, immigrant, diabetes onset

Introduction

The Middle East is one of the five areas in the world where type 2 diabetes prevalence is especially high [1]. Migration and urbanization are established risk factors for type 2 diabetes and cardiovascular disease [2-4]; and in the population based MEDIM (Impact of Migration and Ethnicity on Diabetes In Malmö) study, we previously showed that in immigrants from Iraq, the largest non-European immigrant group in Sweden [5], the prevalence of type 2 diabetes is twice that of the native Swedish population (11.6 vs. 5.8 %, $P<0.001$)[6]. Similar diabetes prevalences have previously been reported in other studies conducted amongst immigrants to Sweden from the Middle East (Turkey, Iran, Iraq and Pakistan) and studies of immigrants to Norway from Pakistan [7-9]. Even higher diabetes prevalence rates were reported in a population of Iraqi and Swedish background living in a deprived Swedish neighbourhood [10]. In 2010, immigrants from Iraq and native Swedes living in the socioeconomically deprived neighborhood of Rosengård in Malmö were screened for type 2 diabetes. The prevalence of type 2 diabetes was 20% in both ethnic groups and notably the Swedish population in Rosengård had a 5-fold higher diabetes prevalence compared to the Swedish population in general [11]. These data are consistent with studies from the United Kingdom reporting the diabetes prevalence amongst adult Europeans, Pakistanis and African Caribbeans to exceed 20%, where relative poverty, obesity and physical inactivity are likely contributors [12].

Age at diabetes onset also varies across ethnicities, with, for instance, diabetes onset in Mexicans and Jamacans [13] and Pima Indians from the United States [14] often being in adolescence and early adulthood. In the United Kingdom, diabetes onset occurs almost 10 years earlier in non-white populations (i.e. Black African, Caribbean or South Asian ethnicity) than in Whites [15]. Moreover, Israeli Arabs are at higher risk of diabetes and are also reported to be younger at diabetes onset than Israeli Jews [16].

Early age of diabetes onset is associated with a particularly poor prognosis, most notably with regard to diabetic complications and rapidly declining glycaemic control [17]. Recently results from the National Health and Nutrition Examination Study revealed that earlier diabetes onset is associated with worse glucose regulation [18] and conclude that aggressive individualized treatment could benefit this higher risk group.

Diabetes accounts for over 8% of excess mortality in the Middle East [19]. Studies of long-term glycaemic control as assessed by HbA1c in ethnically diverse diabetes-free populations are scarce, and thus it is important to identify

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risk factors that are associated with poor glycaemic control before the onset of diabetes in high risk ethnically diverse populations. This would help inform evidence-based guidelines on how to best identify persons at risk and help optimize preventive interventions for these high-risk groups. In this population-based survey of Iraqi immigrants to Sweden, we compared age of diabetes onset with that observed in native Swedes. Furthermore, in a subsample of participants without previously diagnosed diabetes, we examined the factors that explained differences in glycaemic control (HbA1c) in immigrants from Iraq compared to native Swedes.

Methods

Participants

Individuals born in Iraq represent the largest immigrant group in Malmö, Sweden, collectively accounting for almost 9,000 of the City's ~300,000 inhabitants [5]. According to the census register, the population of Iraqi immigrants 30 to 75 years of age in Malmö consisted in 2010 of 4,397 persons with a mean age of 44.8 years and of whom 57.8% were men. Swedish born citizens living in the same geographical area in Malmö were randomly selected from the census register to reach a similar age and gender distribution as the Iraqi population (mean age 45.2 years, *P*=0.08; 57.4% males *P*=0.74). Iraqi and Swedish individuals were then contacted and invited by mail and phone to participate in the study. We aimed to recruit a final sample of 2:1 Iraqi and Swedish participants with the goal to reach a similar age and sex distribution amongst the final participants as amongst the original background population (see Table 1).

Compared to the eligible study population meeting the inclusion criteria (Iraqis n=2894; Swedes n=2364), Iraqi men and women had a participation rate of 45.9 and 52.1% respectively, compared with 32.2 and 31.8% respectively in Swedish participants (see supplementary figure).

All individuals who were invited to participate were also asked if they had previously been diagnosed with type 1 or type 2 diabetes. People with type 1 diabetes, or **severe** physical or mental illness or disabilities were excluded from the study. To minimize assessment biases, examinations were conducted within a relatively short timeframe (February 1, 2010 through December 31, 2012).

Physical examination

The investigation took place at Skåne University Hospital, Malmö, Sweden. Swedish- and Arabic-speaking research

nurses conducted standard physical examinations. Assessments of standard physical and clinical variables such as blood pressure, height, weight, waist circumference and BMI were performed as described previously [10]. Normal weight was defined as BMI<25 kg/m^2, overweight as BMI ≥25 and <30 kg/m^2 and obesity as BMI ≥30 kg/m^2 [20]. Abdominal obesity was defined as a waist circumference of ≥94 cm in men and ≥80 cm in women, as recommended for Middle Eastern and white populations by the International Diabetes Federation/American Heart Association/National Heart Lung and Blood Institute [21].

Blood samples and oral glucose tolerance test (OGTT)

Participants were instructed to abstain from food, fluids (except water) and tobacco from after 10 pm the night before testing; they were also asked to bring a record of their current medications to the examination. The following morning, a 75-g OGTT was performed. Blood samples were collected prior to glucose loading and at 30, 60, 90 and 120 min thereafter; glucose was measured in fresh plasma from venous whole blood immediately after sampling using a photometer (HemoCue AB, Ängelholm, Sweden) as described previously [10]. Plasma insulin, total cholesterol, triglyceride (p-TG), high-density lipoprotein (p-HDL), low-density-lipoprotein (p-LDL) and HbA1c levels were determined as previously described [10, 22].

Normal glucose tolerance (NGT) was defined as fasting glucose levels of <6.1 mmol/l and 2-h plasma glucose <7.8 mmol/l. Isolated impaired fasting glucose (IFG) was defined as fasting plasma glucose ≥6.1 mmol/l and <7.0 mmol/l and a 2-h plasma glucose level of <7.8 mmol/l [23]. Isolated impaired glucose tolerance (IGT) was defined as a fasting plasma glucose level of <6.1 mmol/L and a 2-h plasma glucose level of ≥7.8 mmol/l and <11.1 mmol/l [23]. IFG in combination with IGT was defined as impaired glucose regulation [23].

Type 2 diabetes was diagnosed by a fasting plasma glucose level of ≥7.0 mmol/l and/or by a 2-h plasma glucose level of ≥11.1 mmol/l. Two values on separate occasions exceeding these thresholds were needed for diagnosis [23]. If only one glucose value was indicative, the OGTT was repeated on another day within 2 weeks with the same procedures.

In participants stating they had previously diagnosed diabetes, the diagnosis was confirmed by examining their prescription of oral hypoglycaemic agents (OHAs) and/or insulin, or by a fasting glucose concentration of ≥7.0 mmol/l. These participants were asked what year they were diagnosed with diabetes. They did not undergo an

OGTT. Participants who were not on OHAs and/or insulin and who had a FPG level of <7.0 mmol/l did undergo an OGTT.

Questionnaires

Information on lifestyle habits, previous diagnosis of diabetes, current medication, family history of diabetes (FH) and sociodemography was collected in interviews by Arabic- and Swedish-speaking nurses using structured questionnaires in Swedish or Arabic depending on the participant's mother tongue. All questionnaires were translated and back-translated by two independent professional translators with Arabic as their native language [10].

First-degree FH was considered as the presence of diabetes in biological parents, siblings and/or children: FH- (no first-degree relatives), FH+ (one first-degree relative) and FH++ (two or more first-degree family relatives with diabetes, i.e. family clustering). Smoking habits: non-smokers included never-smokers and participants who had stopped smoking more than 6 months previously. All others were considered active smokers [24]. Alcohol consumption: participants who drank alcohol were considered alcohol consumers, regardless of how often or how much they stated they drank. Physical activity (PA) was estimated using questions developed by the Swedish National Board of Health and Welfare to estimate time spent physically active [25]. Time spent doing non-strenuous PA (e.g., walking, cycling or gardening) and strenuous PA (e.g., jogging, swimming, basketball or football) was estimated by the participants in minutes. Time spent doing strenuous PA was multiplied by two and then added to time spent doing non-strenuous PA [25]. Education level was categorized as (1) high school or less (≤HS) or (2) above HS. Economic difficulties: difficulties in paying for food, rent or bills on one or several occasions during the last 12 months [5].

Statistical analysis

Analyses were performed using STATA IC/12.1. In this study the primary outcome was age at diabetes onset and the secondary outcome was level of HbA1c (in mmol/mol). Characteristics were compared between people born in Iraq and those born in Sweden, after adjusting for age and sex, using linear regression for continuous outcome variables and logistic regression for binary outcome variables. Age at diabetes onset was plotted using Kaplan–Meier survival curves, and the differences between the survival curves was assessed using the log-rank test (Figure

2a and 2b). Cox regression was used to study age at diabetes onset. The underlying unit of time in the Cox model was the participant's age (years) and the event variable was age at diabetes diagnosis (years) (Table 2). The proportionality assumptions of the Cox models were assessed using time-dependent interaction terms and found to hold.

The covariates studied in the Cox regression were sex, country of birth, FH, obesity, education level and height respectively; height was included as short stature conveys higher risk of diabetes susceptibility in ethnic non-European minority groups [26]. To control for confounding, independent variables associated with diabetes onset in univariate analyses (*P*-value of 0.05 or less) were entered into the multivariable regression analysis, except for sex which was forced into the model regardless of its degree of association with diabetes in univariate analyses (Table 2).

In participants without previously diagnosed diabetes, associations with HbA1c were assessed; independent variables associated with HbA1c in univariate analyses with *P*-value of 0.05 or less were studied in multivariable stepwise linear regression analysis, the results of which are expressed as β coefficients with 95% confidence intervals (CIs) (Table 3). HbA1c was log_{10}-transformed before analysis to approximate a normal distribution. Regression coefficients for the continuous independent variables were standardized in the strata of ethnicity and sex using the z-score transformation (with a mean of 0 and standard deviation (SD) of 1). The transformed variable is thus expressed in SD units. To control for the putative confounding effects of ethnicity and sex, we performed the z-score transformations within these strata. Study participants with missing data were excluded from the regression analysis. Tests for interactions of all independent variables included in the Cox regression and linear regression models were performed to determine if these variables modified the primary associaitons of interest (Table 2 and Table 3).

All tests were two-sided and a *P*-value of <0.05 was considered statistically significant.

A variance inflation factor (VIF) of 10 or above may indicate multicollinearity [27], but since all VIF values in the final multivariate regression models were <3.4 this was not considered an issue in this study. Power calculation was based on estimations on differences inT2D in an adult Swedish and Iraqi population. From previous studies we estimated that the T2D prevalence would be 7% in a Middle Eastern population and 4% in native Swedes [8]. With alpha = 0.05 (two-sided test) and a power of 80% we would detect a significantdifference in T2D prevalence with a

sample size of 1398 participants born in Iraq and 699 born in Sweden.

Ethical considerations

All participants provided written informed consent and the Ethics Committee at Lund University approved the study (application nos. 2009/36 and 2010/561). This investigation conforms to the principles outlined in the Declaration of Helsinki [28].

Results

In this cross-sectional study of Iraqi-born (N=1398) compared with Swedish-born participants (N=757), type 2 diabetes was more than twice as prevalent (11.6 vs. 5.8%, $p<0.001$) and FH was more than twice as common (Table 1). Moreover, a strong FH, with ≥2 members with diabetes (FH++), was more than six times more prevalent in Iraqi- vs. Swedish-born individuals (Table 1). In addition, obesity (BMI ≥30 kg/m^2) and abdominal obesity were highly prevalent amongst Iraqis (obesity: 37.5% vs. 23.0%, $P<0.001$; abdominal obesity (77.5% vs. 67.4%, $P<0.001$) (Table 1). Diabetes prevalence by ten-year age group in participants born in Iraq or Sweden is illustrated in Figure 1. The prevalence of type 2 diabetes increased with increasing age and was at least twice as high in Iraqis versus Swedes in almost all ten-year age groups. In Iraqis the prevalence exceeded 18% in participants 50 years and older and was highest in participants 60 years and older, with a prevalence of 34.2% vs. 15.0 % in Swedes, $P<0.001$ (Figure 1).

Age at diabetes onset and risk of diabetes

Diabetes onset occurred six years earlier in immigrants from Iraq (47.6 vs. 53.4 years, $P<0.001$). Iraqi ethnicity independently raised the hazards for diabetes onset. However, the hazards were heavily influenced not only by ethnicity, but also by FH and obesity (Table 2 & Figure 2a and 2b) (data adjusted for sex).There was an interaction between family history and obesity, $P_{interaction}$=0.001 and the effect of an extended FH of diabetes (FH++) in combination with obesity conveyed a 5.1-fold (95% CI 3.2-8.2) increased hazards ratio, as compared to non-obese, FH- participants. These data also indicate that non-obese FH++ participants had a slightly higher hazard ratio for disease onset than obese FH- participants (Table 2).

Glycaemic control in participants free from diabetes

The level of HbA1c was marginally higher in Iraqis than in Swedes, after adjustment for age and sex (Table 1). This difference was also apparent in participants without previously known diabetes (Iraqis N=1270; Swedes N=728; 4.5% (36.1 mmol/mol) vs. 4.4% (35.6 mmol/mol), P=0.038), in age- and sex-adjusted data.

We observed that a higher proportion of the participants with FH++ had HbA1c values ≥5.0% (42 mmol/mol), highlighting this group as one at especially high risk of diabetes [29]: FH- 8.6%, FH+ 9.7%, FH++ 17.9 %, $P_{\text{for trend}}$ <0.001 (age- and sex-adjusted data). HbA1c by age groups, country of birth and FH is shown in Figure 3. In general, HbA1c increased with age but in a manner that is dependent on country of birth and FH of diabetes: the HbA1c levels were highest in almost all age groups for FH++ participants, followed by participants born in Iraq and FH+ participants. Swedes in all age groups had lower HbA1c levels compared with Iraqis (Figure 3).In participants not previously diagnosed with diabetes, being born in Iraq was strongly associated with higher HbA1c levels, irrespective of age, sex, BMI, waist circumference, physical activity, socioeconomic factors and type 2 diabetes diagnosed at OGTT (Table 3). The stepwise regression in Models IV to VI shows that irrespective of adjustment for traditional factors influencing glycaemic control other than sex and age, the association between country of birth and HbA1c was offset when FH was included in the model (Table 3). In the final Model VI, all risk factors explained 26% of the variance (R^2) in HbA1c (Table 2a). The variance did not differ between ethnicities (data not shown). There were no interactions in the model.

Representativeness of the study sample

Comparisons with the background population revealed that the gender distribution amongst the final Iraqi participants remained consistent (57.8%), however the proportion of male Swedish participants was somewhat lower as compared to the background population (52.8 vs. 57.4%, P=0.02). Further, the Iraqi and Swedish participants were slightly older as compared to the background population (Iraqis 46.2 vs. 44.8 years, P<0.001; Swedes 49.5 vs. 45.2 years, P<0.001). The prevalence of self-reported type 2 diabetes in participants versus the eligible population meeting the inclusion criteria did not differ significantly (data not shown).

Discussion

Key findings

Studies of long-term glycaemic control in non-diabetic populations are scarce. This study contributes novel data that immigrants from the Middle East without previously diagnosed diabetes have poorer glycaemic control than ethnic Swedes. Furthermore, the difference in glycaemic control in Iraqis versus Swedes is primarily attributable to extended FH of diabetes, rather than to older age, higher BMI or larger waist circumference. We also show that independent of FH or obesity, Iraqis have an earlier age of diabetes onset and that the risk of diabetes onset is higher in Middle Eastern immigrants. Our study also shows that diabetes onset due to FH is augmented by obesity.

Diabetes onset

Previous studies of non-European immigrants to Sweden revealed a type 2 diabetes prevalence of about 15% amongst 60-year-old men and women [30], which is half the prevalence reported in this survey. Differences compared to this study could be attributable to differences in the sizes of the investigated populations (1398 vs. 123 non-European immigrants), but also the fact that the results of Wändell et al were collected between 1997 and 1999, i.e. more than a decade earlier than our results. Previously in the MEDIM study we showed that of those Iraqi immigrants to Sweden who have not yet developed diabetes, a large proportion are expected to do so within the next decade [6]. Thus our data is likely to reflect a growing diabetes prevalence in this non-European immigrant population.

Others have reported ethnic differences in age at diabetes onset, reporting, for instance, early onset in populations from central America (Mexico) and the Caribbean (Jamaica) [13], as well as in minority populations of Pima Indians in the United States [14]. Furthermore, a study from the UK reported that non-White populations (i.e. Blacks, Caribbeans and South Asians) have an earlier onset than Whites [15] and a study from Israel reported that Arabs have an earlier onset than Jews [16]. These results showing ethnic differences in diabetes onset are in accordance with our findings of an earlier disease onset in the Middle Eastern population as compared to native Swedes, despite the younger mean age of the participants in this group. Although others have reported that individuals with FH of diabetes have an earlier diabetes onset as compared to those without FH [31], our data contributes novel findings that Iraqi background, FH and obesity are independent risk factors for early onset. Further our study shows that

FH++ may be a slightly stronger contributor to early disease onset than obesity and that diabetes onset due to FH is augmented by obesity. Thus, because obesity is a modifiable risk factor, it is likely that weight loss interventions for diabetes prevention could be especially important in this population with a high prevalence of extended FH of diabetes.

Glycaemic control and preventive actions

It is reported that diabetes patients migrating from the Middle East often present with a high degree of microvascular and macrovascular complications at a relatively young age compared with native Swedes [22, 32] and that age at diabetes onset is associated with worse subsequent glycaemic control [18]. Consequently, we hypothesized that glycaemic control, as estimated by HbA1c, in this immigrant population with early diabetes onset would be worse as compared to a population with later onset. Few studies have assessed long-term glycaemic control in ethnically diverse non-diabetic populations. Our data confirms that in participants not previously diagnosed with diabetes, the Iraqis have worse glycaemic control as compared to Swedes. Further, in this survey almost 20% of FH++ individuals had HbA1c levels of >42 mmol/mol, indicating a high risk of diabetes, as proposed by recent studies [29]. To the best of our knowledge this is the first study showing that ethnic differences in glycaemic control are explained by extended FH of diabetes rather than by other traditional risk factors such as age, sex, excess weight, larger waist circumference, type 2 diabetes, physical inactivity or socioeconomy.

Early detection of elevated levels of HbA1c would indicate the need for intensive lifestyle interventions to prevent the early disease onset [29]. The Diabetes Prevention Program has shown that lifestyle interventions are more efficient in preventing type 2 diabetes than medication with metformin [33]. That study is being conducted in a western population with a low prevalence of FH of diabetes. Since our data suggests that glycaemic control in the non-diabetic stages is strongly influenced by family clustering, our study highlights the need for preventive studies targeting individuals with family clustering of diabetes, with emphasis on identifying the optimal medical and non-medical preventive actions against diabetes in this group. However, studies have shown large challenges in addressing lifestyle change in sedentary individuals at familial risk of diabetes [34]. Studies have also reported social and cultural obstacles to increased physical activity in Middle Eastern immigrant female populations [35]. Thus, prevention programs targeting this high-risk group need to address these challenges to be successful [36, 37]

Strengths and limitations

The major strengths of this study are that the study is population-based and represents a large fraction of the Iraqi population in the region, matched to Swedish citizens living in the same geographic and socioeconomic neighborhood. This study is also distinct from other studies of this topic in that it includes OGTT with repeated measurements as well as detailed metabolic phenotyping and assessments of socioeconomy and lifestyle exposures. Another strength is that participants reporting a history of diabetes were only considered as having diabetes if they were currently taking diabetes medication and/or had fasting glucose levels within the limits of diabetes. Studies have shown that diabetes patients from the Middle East are less compliant to treatment than native European patients, which might increase the probability of poor glycaemic control[38]. Thus, when studying glycaemic control, only participants without previously diagnosed diabetes were included to avoid biasing the outcome of our data.

The participants were somewhat older and the proportion of men in the Swedish group was lower than observed in the background population. The study is also limited by the lower participation rate for Swedes than Iraqis, probably reflecting the fact that more Swedes, due to employment, were not able to attend the health exams, which took place on weekday mornings. However, we consider our data reliable since age and sex differences were adjusted for in the models. Another limitation is the cross-sectional, observational design, with the inability to infer causality.

Conclusions

This population-based study of immigrants from the Middle East contributes novel findings showing an earlier diabetes onset and, in those without previously diagnosed diabetes, poorer glycaemic control as compared to the native Swedish population. Furthermore, this study shows that extended FH of diabetes may, independently of other risk factors, explain the poorer glycaemic control as well as the earlier diabetes onset observed in immigrants from the Middle East compared with non-immigrants in Northern Europe.

In clinical settings adult patients from the Middle East should be considered for diabetes using a fairly broad screening criteria focusing on a wide-range of indications, especially those with FH of diabetes and/or obesity. We

conclude that clinical interventions tailored to this high-risk group, particularly those with an extended family history of the disease, may be an appropriate prioritization of health care resources in Northern European countries.

Conflict of interests

The authors declare that they have no conflicts of interests.

Authors' contributions

LB designed the study, wrote the research protocol, obtained, analyzed and interpreted the data, and wrote the manuscript. UL assisted with the design of the study, interpreting the data and writing the manuscript. PWF contributed to interpreting and analyzing the data and writing the manuscript. All authors have revised/edited the article critically and have approved the final version of the manuscript.

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Table 1. Characteristics of participants from Malmö born in Iraq and Sweden.

Variable	Valid measurements N	Iraq N= 1398	Valid measurements N	Sweden N=757	P
		Country of birth			
Age (years)	1398	46.2 (9.6)	757	49.5 (11.2)	<0.001
Age at diabetes onset (years)	162	47.6 (9.7)	44	53.4 (11.9)	0.001
Male sex, *n* (%)	1398	819 (58.6)	757	**400 (52.8)**	0.010
Type 2 diabetes, all cases, *n* (%)	1389	162 (11.6)	753	44 (5.8)	<0.001
Previously known, *n* (%)		118 (8.4)		25 (3.3)	0.101
Newly diagnosed, *n* (%)		44 (3.1)		19 (2.5)	<0.001
First-degree history of diabetes, *n* (%)	1348	723 (51.7)	733	209 (27.6)	<0.001
First-degree history of diabetes, *n* (%)	1348		733		
No relative with diabetes (FH-)		625 (44.7)		524 (69.2)	<0.001
One relative (FH+)		398 (28.5)		182 (24.0)	0.025
≥2 relatives (FH++)		325 (23.2)		27 (3.6)	<0.001
Body mass index (BMI) (kg/m^2)	1397	29.3 (4.5)	752	27.3 (4.7)	<0.001
Weight distribution	1397		752		
Normal weight, BMI <25, *n* (%)		199 (14.3)		269 (35.5)	<0.001
Overweight, BMI 25 to 29.9, *n* (%)		674 (48.2)		314 (41.5)	0.002
Obesity, BMI ≥30, *n* (%)		524 (37.5)		174 (23.0)	<0.001
Waist circumference men (cm)	1392	99.3 (11.5)	753	97.8 (11.68)	0.002
Waist circumference women (cm)	1393	93.2 (11.5)	753	89.2 (14.07)	<0.001
Abdominal obesity (men ≥94 cm; women ≥80 cm)	1387	1083 (77.5)	749	510 (67.4)	<0.001
b-HbA1c (%)	1345	4.6 (0.9)	738	4.5 (0.8)	<0.001
b-HbA1c (mmol/mol)	1345	37.9 (10.1)	738	36.4 (8.3)	<0.001
Fasting glucose (mmol/l)$^{\pm}$	1396	5.9 (1.5)	754	5.7 (1.2)	0.078
2-hour glucose (mmol/l)$^{\pm}$	1260	6.1 (2.4)	722	6.0 (2.4)	0.002
Total cholesterol (mmol/l)$^{\neq}$	1346	4.9 (0.9)	733	5.2 (1.0)	<0.001
p-LDL (mmol/l)$^{\neq}$	1314	3.2 (0.8)	702	3.3 (0.9)	<0.001
p-HDL (mmol/l)$^{\neq}$	1348	1.2 (0.3)	732	1.4 (0.4)	<0.001
p-TGs (mmol/l)$^{\neq}$	1345	1.6 (1.2)	735	1.3 (0.8)	<0.001
Physical activity <150 minutes/week, *n* (%)	1342	915 (72.0)	756	279 (38.3)	<0.001

Alcohol consumers, *n* (%)	1348	204 (14.6)	741	598 (79.0)	<0.001
Education level ≤HS, *n* (%)	1382	385 (27.5)	752	143 (18.9)	<0.001
Economic difficulties on one or several occasions in the last 12 months, *n* (%)	1391	717 (51.3)	752	115 (15.2)	<0.001

Crude data are presented as means (standard deviation, SD) or numbers (percentages). Differences in means between groups were adjusted for age and sex using linear regression models (for continuous variables), while differences in proportions between groups (except for male sex and family history of diabetes) were studied using logistic regression adjusted for age and sex.

All tests were two-sided and a *P*-value of <0.05 was considered statistically significant.

[±] Differences were also adjusted for medication with oral hypoglycaemic agents and/or insulin.

[♯] Differences according to country of origin were also adjusted for treatment with medication lowering cholesterol levels (i.e. statins or similar medication).

Abbreviations: FH, first-degree family history of diabetes (biological parents, children and/or siblings) in no (FH-), one (FH+) or ≥2 relatives (FH++); HDL, high-density lipoprotein; HS, high school; LDL, low-density lipoprotein; SD, standard deviation; TG, triglyceride

Table 2. Hazards for diabetes onset in immigrants from Iraq (N=1398) compared with native Swedes (N=757) assessed by univariate and multivariate Cox regression. The underlying unit of time was the participant's age (years) and the event variable was age at diabetes diagnosis (years). Data presented as hazard ratios with 95% confidence intervals (CI).

	Unadjusted[+] hazard ratio	95% CI	Hazard ratio[++]	95% CI
Born in Sweden, reference	1.0		1.0	
Born in Iraq	3.3	2.4 to 4.6	2.2	1.5 to 3.2
Female sex, reference	1.0		1.0	
Male sex	1.3	0.9 to 1.7	1.2	0.9 to 1.6
Height (cm), per 1 SD	0.9	0.9 to 1.0	-	
Education level ≤HS	0.9	0.7 to 1.3	-	
Family history of diabetes and obesity (BMI ≥30 kg/m^2)				
- No family history (FH-), no obesity, reference	1.0		1.0	
- One first-degree relative (FH+), no obesity	1.7	1.1 to 2.9	1.6	0.9 to 2.6
- Two or more first-degree relatives (FH++), no obesity	3.8	2.3 to 6.2	2.8	1.7 to 4.7
- No family history (FH-), obesity	2.6	1.6 to 4.1	2.4	1.5 to 3.8
- One first-degree relative (FH+), obesity	3.7	2.2 to 6.1	2.9	1.7 to 4.9
- Two or more first-degree relatives (FH++), obesity	7.1	4.5 to 11.2	5.1	3.2 to 8.2

[+] The univariate model included country of birth, sex, FH, obesity, education level and height, the latter a proxy for diabetes susceptibility in ethnic non-European minority groups [26]. [++] In the multivariable model, variables associated with diabetes onset in univariate analyses were entered, except for sex which was forced into the model.

Table 3. Risk factors associated with higher HbA1c levels ($\log_{10}$-transformed) in immigrants from Iraq and native Swedes without previously diagnosed diabetes (Iraqis N=1270; Swedes N=728). Associations are expressed as β coefficients with 95% confidence intervals.

	Univariate Model β (95% CI)	Model 1 N=1937 R^2 0.08 β (95% CI)	Model II N=1923 R^2 0.12 β (95% CI)	Model III N=1923 R^2 0.25 β (95% CI)	Model IV N=1872 R^2 0.09 β (95% CI)	Model V N=1859 R^2 0.13 β (95% CI)	Model VI N=1859 R^2 0.26 β (95% CI)
Born in Iraq	.006 (-.001 to .012)	**.007** (.001 to .013)	**.008** (.002 to .013)	**.006** (.001 to .012)	.004 (-.002 to .011)	.005 (-.001 to .011)	.005 (-.001 to .011)
Age (years), per 1 SD	**.021** (.017 to .024)	**.021** (.018 to .024)	**.016** (.014 to .019)	**.017** (.014 to .019)	**.020** (.017 to .023)	**.018** (.015 to .021)	**.017** (.014 to .020)
Male sex	**.010** (.003 to .016)	**.010** (.004 to .016)	**.007** (.002 to .012)	**.008** (.002 to .013)	**.011** (.005 to .017)	**.011** (.005 to .017)	**.009** (.003 to .014)
Waist circumference, per 1 SD	**.017** (.014 to .021)		**.009** (.004 to .013)	**.008** (.003 to .014)		**.012** (.006 to .017)	**.007** (.001 to .012)
Body mass index (kg/m^2), per 1 SD	**.014** (.011 to .017)		.002 (-.003 to .007)	.002 (-.003 to .007)		.002 (-.004 to .008)	**.002** (-.003 to .007)
Education level ≤HS	**.018** **(.010 to .027)**			.007 (.001 to .013)			.006 (-.001 to .012)
Type 2 diabetes diagnosed at OGTT	**.171** (.177 to .188)			**.154** (.138 to .170)			**.152** (.135 to .169)
Family history of diabetes One first-degree relative (FH+)	**.010** (.003 to .017)				**.009** (.002 to .016)	**.008** (.001 to .015)	**.006** (.001 to .013)
Two or more first-degree relatives (FH++)	**.019** (.010 to .028)				**.013** (.004 to .023)	**.011** (.002 to .020)	**.010** (.002 to .018)

β-coefficients were standardized (SD) in the strata of ethnicity and sex per 1 SD unit of variance for the continuous independent variables. Multicollinearity, Variance Inflation Factor (VIF) < 3.4. Physical activity h/week, per 1 SD and economic difficulties at least once in the last year were not independently associated with HbA1c in the univariate model (data not shown) and were thus not included in the multivariate analysis. Bold-faced numbers are statistically significant.

Figure legends:

Figure 1. Diabetes prevalence in relation to 10-year age group in participants born in Iraq or Sweden. Diabetes increased with age but was more prevalent in Iraqis than Swedes at ages of 50 years and older. The data are adjusted for sex.

Figure 2a and 2b. Percentage of participants free from diabetes in relation to country of birth *P*<0.001; log-rank test (Figure 2a) and in relation to family history of diabetes in no (FH-), one (FH+) and two or more first-degree relatives (FH++) *P*<0.001; log-rank test (Figure 2b). Data were culled at the 90th percentile.

Figure 3. HbA1c (mmol/mol) in relation to age, first-degree family history of diabetes and country of birth in participants without previously diagnosed diabetes (born in Iraq N=1270; born in Sweden N=728). Data for age groups 55 years and older were collapsed due to the small groups for ages 60 years and older (N<23). FH-, no first-degree relative with diabetes; FH+, one first-degree relative with diabetes; FH++, two or more first-degree relatives with diabetes.