Original article

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

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Abstract

Aims. – Immigrant populations from the Middle East develop diabetes earlier than indigenous European populations; however, the underlying etiology is poorly understood. This study looked at the risk factors associated with early diabetes onset and, in non-diabetics, glycaemic control in immigrants from Iraq compared with native Swedes.

Methods. – This cross-sectional population-based study comprised 1398 Iraqi immigrants and 757 Swedes (ages 30–75 years) residing in the same area of Malmö, Sweden. Outcomes were age at diabetes onset and glycaemic control (HbA1c) as assessed by Cox proportional hazards and linear regression, respectively.

Results. – In Iraqis vs Swedes, clustering in the family history (in two or more relatives) was more prevalent (23.2% vs 3.6%, P < 0.001) and diabetes onset occurred earlier (47.6 years vs 53.4 years, P = 0.001). Having an Iraqi background independently raised the hazard ratio (HR) for diabetes onset. Diabetes risk due to family history was augmented by obesity, with the highest HRs observed in obese participants with clustering in the family history (HR; 5.1, 95% CI 3.2–8.2) after adjusting for country of birth and gender. In participants without previously diagnosed diabetes (Iraqis; n = 1270; Swedes: n = 728), HbA1c levels were slightly higher in Iraqis than in Swedes (4.5% vs 4.4%, P = 0.038). This difference was explained primarily by clustering in the family history rather than age, obesity, lifestyle or socioeconomic status.

Conclusion. – The study shows that the greater predisposition to diabetes in Middle Eastern immigrants may be explained by a more extensive family history of the disorder; clinical interventions tailored to Middle Eastern immigrants with such a family history are thus warranted.

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Keywords: Heredity; Hyperglycaemia; Middle East; Immigrant; Diabetes onset

1. Introduction

The Middle East is one of five areas in the world where type 2 diabetes (T2D) prevalence is especially high [1]. Migration and urbanization are established risk factors for T2D and cardiovascular disease [2–4]; and in the previous population-based MEDIM (Impact of migration and ethnicity on diabetes in Malmö) study, we showed that, in immigrants from Iraq, the largest non-European immigrant group in Sweden [5], the prevalence of T2D is twice that of the native Swedish population (11.6% vs 5.8%, P < 0.001) [6]. Similar diabetes prevalences have been reported in other studies conducted in immigrants to Sweden from the Middle East (Turkey, Iran, Iraq and Pakistan) and in studies of immigrants to Norway from Pakistan [7–9].
Even higher diabetes prevalence rates were reported in a population with Iraqi and Swedish backgrounds living in a deprived Swedish neighbourhood [10]. In 2010, immigrants from Iraq and native Swedes living in the socioeconomically deprived neighbourhood of Rosengård in Malmö were screened for T2D. The prevalence was 20% in both ethnic groups and, notably, the Swedish population in Rosengård had a fivefold higher diabetes prevalence compared with the Swedish population in general [10]. These data are consistent with studies from the United Kingdom (UK), reporting that the diabetes prevalence among adult Europeans, Pakistanis and African Caribbeans exceeds 20%, and that relative poverty, obesity and physical inactivity are likely contributors [11].

Age at diabetes onset also varies across ethnicities with, for instance, diabetes onset in Mexicans and Jamaicans [12] and Pima Indians in the United States (US) [13] often being in adolescence and early adulthood. In the UK, diabetes onset occurs almost 10 years earlier in non-white populations (Black African, Caribbean and South Asian ethnicities) than in whites [14]. Moreover, Israeli Arabs are at higher risk of diabetes and are also reported to be younger at diabetes onset than Israeli Jews [15].

An early age of diabetes onset is associated with a particularly poor prognosis, most notably with regard to diabetic complications and rapidly declining glycaemic control [16]. Recently, results from the US National Health and Nutrition Examination Survey (NHANES) revealed that earlier diabetes onset is associated with poorer glucose regulation [17] and concluded that aggressive individualized treatment could benefit this higher-risk group.

Diabetes accounts for over 8% of excess mortality in the Middle East [18]. However, 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 the risk factors associated with poor glycaemic control before the onset of diabetes in high-risk ethnically diverse populations. This would help to inform evidence-based guidelines on how best to identify those at risk and help to optimize preventative interventions for these high-risk groups. In the present population-based survey of Iraqi immigrants in Sweden, the age of diabetes onset was compared with that observed in native Swedes. Also, in a subsample of participants without previously diagnosed diabetes, the factors that explained differences in glycaemic control (HbA1c) in immigrants from Iraq compared with native Swedes were also examined.

2. Methods

2.1. Participants

Individuals born in Iraq represent the largest immigrant group in Malmö, Sweden, collectively accounting for almost 9000 of the city’s ~300,000 inhabitants [5]. According to the census register, the population of Iraqi immigrants aged 30–75 years in Malmö in 2010 consisted of 4397 people with a mean age of 44.8 years, 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 obtain a similar age and gender distribution as the Iraqi population (mean age 45.2 years, \( P = 0.08; 57.4\% \) males, \( P = 0.74 \)). These Iraqi and Swedish individuals were then contacted by post and phone, and invited to participate in the study. The goal was to recruit a final sample of 2:1 Iraqi and Swedish participants to reach a similar age and gender distribution in the final study participants as in the original background population (Table 1).

Considering the eligible study population that met the inclusion criteria (Iraqis = 2894; Swedes = 2364), Iraqi men and women had a participation rate of 45.9% and 52.1%, respectively, compared with 32.2% and 31.8%, respectively, of the Swedish participants (Fig. S1, Supplementary data). All individuals invited to participate were also asked if they had previously been diagnosed with either type 1 diabetes or T2D. 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 (1 February 2010 through 31 December 2012).

2.2. Physical examination

The investigation took place at Skåne University Hospital in Malmö. 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 Body Mass Index (BMI) were performed as described previously [10]. Normal weight was defined as BMI < 25 kg/m\(^2\), overweight as BMI > 25 kg/m\(^2\) but < 30 kg/m\(^2\), and obesity as BMI ≥ 30 kg/m\(^2\) [19]. Abdominal obesity was defined as a waist circumference ≥ 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 [20].

2.3. Blood samples and oral glucose tolerance tests (OGTTs)

Participants were instructed to abstain from food, fluids (except water) and tobacco from 10 pm the night before the test; they were also asked to bring a record of their current medications. 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, Angelholm, 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 [10,21].

Normal glucose tolerance (NGT) was defined as fasting glucose levels < 6.1 mmol/L and a 2-h plasma glucose < 7.8 mmol/L. Isolated impaired fasting glucose (IFG) was defined as fasting plasma glucose ≥ 6.1 mmol/L but < 7.0 mmol/L, and a 2-h plasma glucose < 7.8 mmol/L [22]. Isolated impaired glucose tolerance (IGT) was defined as fasting plasma
Table 1  
Characteristics of study participants living in Malmö, but born in Iraq and in Sweden.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Valid measurements (n)</th>
<th>Iraq (n = 1398)</th>
<th>Valid measurements (n)</th>
<th>Sweden (n = 757)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1398</td>
<td>46.2 (9.6)</td>
<td>757</td>
<td>49.5 (11.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at diabetes onset (years)</td>
<td>162</td>
<td>47.6 (9.7)</td>
<td>44</td>
<td>53.4 (11.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>1398</td>
<td>819 (58.6)</td>
<td>757</td>
<td>400 (52.8)</td>
<td>0.010</td>
</tr>
<tr>
<td>Type 2 diabetes, all cases, n (%)</td>
<td>1389</td>
<td>162 (11.6)</td>
<td>753</td>
<td>44 (5.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previously known, n (%)</td>
<td>1389</td>
<td>118 (8.4)</td>
<td>753</td>
<td>25 (3.3)</td>
<td>0.101</td>
</tr>
<tr>
<td>Newly diagnosed, n (%)</td>
<td>1389</td>
<td>44 (3.1)</td>
<td>753</td>
<td>19 (2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>First-degree FH of diabetes, n (%)</td>
<td>1348</td>
<td>723 (51.7)</td>
<td>733</td>
<td>209 (27.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No relative with diabetes (FH−)</td>
<td>625 (44.7)</td>
<td>524 (69.2)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One relative (FH+)</td>
<td>398 (28.5)</td>
<td>182 (24.0)</td>
<td>0.025</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two or more relatives (FH++)</td>
<td>325 (23.2)</td>
<td>27 (3.6)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1397</td>
<td>29.3 (4.5)</td>
<td>752</td>
<td>27.3 (4.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Crude data are presented as means (SD) or as numbers (percentages); differences in means between groups were adjusted for age and gender using linear regression models (for continuous variables); differences in proportions between groups (except for male gender and family history of diabetes) were studied using logistic regression adjusted for age and gender; all tests were two-sided; P < 0.05 was considered statistically significant; FH: family history (biological parents, children and/or siblings); BMI: body mass index; LDL/HDL: low-density/high-density lipoprotein; HS: high school.

a Differences also adjusted for medication with oral hypoglycaemic agents and/or insulin.
b Differences by country of origin also adjusted for cholesterol-lowering medications (statins or similar drugs).

2.4. Questionnaires

Information on lifestyle habits, previous diagnosis of diabetes, current medication, family history (FH) of diabetes and sociodemographics was collected through 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 whose native language was Arabic [10].

First-degree FH was defined as the presence of diabetes in biological parents, siblings and/or children, and categorized as FH− (no first-degree relatives), FH+ (one first-degree relative) and FH++ (two or more first-degree family relatives with diabetes – in other words, family clustering). Smoking habits were divided into non-smokers, including never-smokers and participants who had stopped smoking more than 6 months previously,
Table 2
Hazard ratios (HRs) for diabetes onset in immigrants from Iraq (n = 1398) compared with native Swedes (n = 757), as assessed by univariate and multivariate Cox regression models.

<table>
<thead>
<tr>
<th>Family history (FH) of diabetes and obesity (BMI ≥ 30 kg/m²)</th>
<th>Unadjusted HR&lt;sup&gt;a&lt;/sup&gt;</th>
<th>95% CI</th>
<th>HR&lt;sup&gt;b&lt;/sup&gt;</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No family history (FH–), no obesity (reference)</td>
<td>1</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>One first-degree relative (FH+), no obesity</td>
<td>1.7</td>
<td>1.1–2.9</td>
<td>1.6</td>
<td>0.9–2.6</td>
</tr>
<tr>
<td>Two or more first-degree relatives (FH++), no obesity</td>
<td>3.8</td>
<td>2.3–6.2</td>
<td>2.8</td>
<td>1.7–4.7</td>
</tr>
<tr>
<td>FH–, obesity</td>
<td>2.6</td>
<td>1.6–4.1</td>
<td>2.4</td>
<td>1.5–3.8</td>
</tr>
<tr>
<td>FH+, obesity</td>
<td>3.7</td>
<td>2.2–6.1</td>
<td>2.9</td>
<td>1.7–4.9</td>
</tr>
<tr>
<td>FH++, obesity</td>
<td>7.1</td>
<td>4.5–11.2</td>
<td>5.1</td>
<td>3.2–8.2</td>
</tr>
</tbody>
</table>

Underlying unit of time was participants’ age (years); event variable was age (years) at diabetes diagnosis.

<sup>a</sup> Univariate model included country of birth, gender, FH, obesity, education level and height, the latter a proxy for diabetes susceptibility in ethnic non-European minority groups [23].

<sup>b</sup> Multivariable model included variables associated with diabetes onset on univariate analyses except for gender, which was forced into the model.

and all others were considered active smokers [23]. Alcohol consumers were defined as participants who drank alcohol, 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 the amount of time spent being physically active [24]. Time spent doing non-strenuous PA (such as walking, cycling and gardening) and strenuous PA (such as jogging, swimming, basketball and football) was estimated by the participants themselves in minutes. Time spent doing strenuous PA was multiplied by two, then added to the time spent doing non-strenuous PA [24]. Education level was categorized as either high school or less (≤ HS) or beyond HS. Economic difficulties were defined as struggling to pay for food, rent or bills on one or several occasions during the past 12 months [5].

2.5. Statistical analysis

Analyses were performed using STATA IC/12.1 software. 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 immigrants born in Iraq and people born in Sweden after adjusting for age and gender, 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 survival curves were assessed using the log-rank test (Fig. 2). 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 (years) at diabetes diagnosis (Table 2). The proportionality assumptions of the Cox models were assessed using time-dependent interaction terms and were found to hold.

Covariates studied in the Cox regression were gender, country of birth, FH, obesity, education level and height; the latter was included because short stature conveys a higher risk of diabetes susceptibility in ethnic non-European minority groups [25]. To control for confounders, all independent variables associated with diabetes onset on univariate analyses (P ≤ 0.05) were entered into the multivariable regression analysis except for gender, which was forced into the model regardless of the degree of association with diabetes on univariate analyses (Table 2).

In participants without previously diagnosed diabetes, associations with HbA₁c were assessed; independent variables associated with HbA₁c on univariate analyses with P values ≤ 0.05 were studied by multivariable stepwise linear regression analysis, the results of which are expressed as β coefficients with a 95% confidence interval (CI; Table 3). HbA₁c was log<sub>10</sub>-transformed before analysis to approximate a normal distribution. Regression coefficients for continuous independent variables were standardized in the strata of ethnicity and gender, using Z-score transformation [with a mean of 0 and standard deviation (SD) of 1]. The transformed variable was thus expressed in SD units. To control for the putative confounding effects of ethnicity and gender, the Z-score transformations were performed within these strata. Study participants with missing data were excluded from the regression analysis. Tests for interactions with all independent variables included in the Cox regression and linear regression models were performed to determine whether these variables modified the primary associations of interest (Tables 2 and 3). All tests were two-sided and P < 0.05 was considered statistically significant.

A variance inflation factor (VIF) ≥ 10 may indicate multicollinearity [26], but because all VIF values in the final multivariate regression models were < 3.4, this was not considered an issue in our study. Power calculation was based on estimations of differences in T2D in the adult Swedish and Iraqi populations. From previous studies, it was estimated that the T2D prevalence would be 7% in the Middle Eastern population and 4% in native Swedes [8]. The alpha level of 0.05 (two-sided test) and power of 80% were expected to detect a significant difference in T2D prevalence with a
Table 3
Risk factors associated with higher HbA1c levels (log10-transformed) in immigrants from Iraq and native Swedes without previously diagnosed diabetes (Iraqis = 1270; Swedes = 728).

<table>
<thead>
<tr>
<th></th>
<th>Univariate model</th>
<th>Model I (n = 1937)</th>
<th>Model II (n = 1923)</th>
<th>Model III (n = 1923)</th>
<th>Model IV (n = 1872)</th>
<th>Model V (n = 1859)</th>
<th>Model VI (n = 1859)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>R² (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
<td>β (95% CI)</td>
</tr>
<tr>
<td>Born in Iraq</td>
<td>0.006 (−0.001–0.012)</td>
<td>0.007 (0.001–0.013)</td>
<td>0.008 (0.002–0.013)</td>
<td>0.006 (0.001–0.012)</td>
<td>0.004 (−0.002–0.011)</td>
<td>0.005 (−0.001–0.011)</td>
<td>0.005 (−0.001–0.011)</td>
</tr>
<tr>
<td>Age (years) per 1 SD</td>
<td>0.021 (0.017–0.024)</td>
<td>0.021 (0.018–0.024)</td>
<td>0.016 (0.014–0.019)</td>
<td>0.017 (0.014–0.019)</td>
<td>0.020 (0.017–0.023)</td>
<td>0.018 (0.015–0.021)</td>
<td>0.017 (0.014–0.020)</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.010 (0.003–0.016)</td>
<td>0.010 (0.004–0.016)</td>
<td>0.007 (0.002–0.012)</td>
<td>0.008 (0.002–0.013)</td>
<td>0.011 (0.005–0.017)</td>
<td>0.011 (0.005–0.017)</td>
<td>0.009 (0.003–0.014)</td>
</tr>
<tr>
<td>Waist circumference per 1 SD</td>
<td>0.017 (0.014–0.021)</td>
<td></td>
<td>0.009 (0.004–0.013)</td>
<td>0.008 (0.003–0.014)</td>
<td>0.012 (0.006–0.017)</td>
<td>0.012 (0.001–0.012)</td>
<td>0.007 (0.001–0.012)</td>
</tr>
<tr>
<td>Body mass index (kg/m²) per 1 SD</td>
<td>0.014 (0.011–0.017)</td>
<td></td>
<td>0.002 (−0.003–0.007)</td>
<td></td>
<td>0.002 (−0.003–0.007)</td>
<td>0.002 (−0.003–0.007)</td>
<td>0.002 (−0.003–0.007)</td>
</tr>
<tr>
<td>Education level ≤ HS</td>
<td>0.018 (0.010–0.027)</td>
<td></td>
<td>0.007 (0.001–0.013)</td>
<td></td>
<td>0.006 (−0.001–0.012)</td>
<td>0.006 (−0.001–0.012)</td>
<td>0.006 (−0.001–0.012)</td>
</tr>
<tr>
<td>Type 2 diabetes diagnosed by OGTT</td>
<td>0.171 (0.177–0.188)</td>
<td></td>
<td>0.154 (0.138–0.170)</td>
<td></td>
<td>0.152 (0.135–0.169)</td>
<td>0.152 (0.135–0.169)</td>
<td>0.152 (0.135–0.169)</td>
</tr>
<tr>
<td>Family history (FH) of diabetes</td>
<td></td>
<td>0.009 (0.002–0.016)</td>
<td>0.008 (0.001–0.015)</td>
<td>0.006 (0.001–0.013)</td>
<td></td>
<td>0.006 (0.001–0.013)</td>
<td></td>
</tr>
<tr>
<td>One first-degree relative (FH+)</td>
<td>0.010 (0.003–0.017)</td>
<td></td>
<td></td>
<td>0.013 (0.004–0.023)</td>
<td>0.011 (0.002–0.020)</td>
<td>0.010 (0.002–0.018)</td>
<td></td>
</tr>
<tr>
<td>Two or more first-degree relatives (FH++)</td>
<td>0.019 (0.010–0.028)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Associations are expressed as β coefficients with 95% confidence intervals (CI); β coefficients were standardized by strata of ethnicity and gender per 1 SD unit of variance for continuous independent variables; multicollinearity variance inflation factor (VIF) < 3.4; physical activity by h/week per 1 SD and economic difficulties at least once in the past year were not independently associated with HbA1c in the univariate model (data not shown) and thus were not included in the multivariate analysis; numbers in boldface are statistically significant.
sample size of 1398 participants born in Iraq and 699 born in Sweden.

2.6. 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). Also, the present investigation conformed to the principles outlined in the declaration of Helsinki [27].

3. Results

In this cross-sectional study of Iraqi-born (n = 1398) compared with Swedish-born (n = 757) participants, T2D was more than twice as prevalent (11.6% vs 5.8%, respectively; P < 0.001) and FH was more than twice as common (Table 1). Also, a strong FH with ≥ two members with diabetes (FH++) was more than six times more prevalent in the Iraqi- vs Swedish-born participants (Table 1). In addition, obesity (BMI ≥ 30 kg/m²) and abdominal obesity in particular were highly prevalent among the Iraqis vs Swedes [obesity: 37.5% vs 23.0%, respectively (P < 0.001); abdominal obesity: 77.5% vs 67.4%, respectively (P < 0.001); Table 1]. Diabetes prevalence by 10-year age groups in participants born in Iraq and Sweden is illustrated in Fig. 1. The prevalence of T2D increased with increasing age and was at least twice as high in Iraqis vs Swedes in almost all 10-year age groups. In Iraqis, the prevalence exceeded 18% in participants aged ≥ 50 years and was highest in participants aged ≥ 60 years, with a prevalence of 34.2% vs 15.0% in Swedes (P < 0.001; Fig. 1).

3.1. Age at diabetes onset and risk of diabetes

Diabetes onset occurred six years earlier in immigrants from Iraq (47.6 vs 53.4 years in native Swedes, P < 0.001). Iraqi ethnicity independently raised the hazard risk (HR) for diabetes onset. However, the HRs were heavily influenced not only by ethnicity, but also by FH and obesity (Table 2 and Fig. 2; data adjusted for gender). There was interaction between FH and obesity (P_interaction = 0.001), and the effect of an extended diabetes FH (FH++) in combination with obesity was a 5.1-fold (95% CI: 3.2–8.2) increased HR compared with non-obese, FH– participants. These data indicated that non-obese FH++ participants also had a slightly higher HR for disease onset than obese FH– participants (Table 2).

3.2. Glycaemic control in participants without diabetes

The level of HbA1c was marginally higher in Iraqis than in Swedes after adjusting for age and gender (Table 1). This difference was also apparent in participants with no previously known diabetes (Iraqi = 1270; Swedes = 728; 4.5% (36.1 mmol/mol) vs 4.4% (35.6 mmol/mol), P = 0.038) in age- and gender-adjusted data.

A greater proportion of participants with FH++ had HbA1c values ≥ 5.0% (42 mmol/mol), thus, highlighting this group as the one with an especially high risk of diabetes [28]: FH–, 8.6%; FH+, 9.7% and FH++ 17.9%; P_trend < 0.001 (age- and gender-adjusted data). HbA1c by age group, country of birth and FH is shown in Fig. 3. In general, HbA1c increased with age, but in a manner dependent on the country of birth and diabetes FH: 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.
3.3. Representativeness of the study sample

Comparison with the background population revealed that the gender distribution of the final Iraqi participants remained consistent (57.8%), although the proportion of male Swedish participants was somewhat lower than in the background population (52.8% vs 57.4%, \( P = 0.02 \)). Furthermore, the Iraqi and Swedish participants were slightly older than the background population (Iraqis: 46.2 years vs 44.8 years, \( P < 0.001 \); Swedes: 49.5 years vs 45.2 years, \( P < 0.001 \)). The prevalence of self-reported T2D in participants vs the total eligible population that met our inclusion criteria did not differ significantly (data not shown).

4. Discussion

4.1. Key findings

Studies of long-term glycaemic control in non-diabetic populations are scarce. The present study contributes novel evidence that immigrants from the Middle East with no previously diagnosed diabetes have poorer glycaemic control than ethnic Swedes. In addition, the difference in glycaemic control in Iraqis vs Swedes is primarily attributable to an extended FH of diabetes rather than older age, higher BMI or larger waist circumference. Our results also show that, independent of FH and obesity, Iraqis immigrants have an earlier age of diabetes onset and a higher risk of diabetes onset. Moreover, our findings show that diabetes onset due to FH is augmented by obesity.
4.2. Diabetes onset

Previous studies of non-European immigrants to Sweden revealed a T2D prevalence of about 15% in 60-year-old men and women [29], which is half the prevalence rate reported in the present survey. Differences in comparison to our survey could be attributable to differences in the sizes of the investigated populations (1398 vs 123 non-European immigrants), but also to the fact that the results of Wändell et al. were collected between 1997 and 1999, more than a decade earlier than our present results. Previously, in the MEDIM study, we showed that, of the Iraqi immigrants to Sweden who had not yet developed diabetes, a large proportion were expected to do so within the next decade [6]. Thus, our present data are 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) [12], as well as in minority populations of Pima Indians in the US [13]. Furthermore, a study from the UK reported that non-white populations (blacks, Caribbeans and South Asians) have an earlier onset than whites [14], and a study from Israel reported that Arabs have an earlier onset than Jews [15]. These results showing ethnic differences in diabetes onset are in accordance with our findings of an earlier disease onset in the Middle Eastern immigrant population compared with native Swedes, despite the younger mean age of the participants in the immigrant group. Although others have reported that individuals with a diabetes FH have an earlier diabetes onset than those without such an FH [30], our data contribute novel findings that Iraqi background, FH and obesity are independent risk factors for early onset. Furthermore, our present 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 an extended diabetes FH.

4.3. Glycaemic control and preventative actions

It has been reported that diabetes patients emigrating from the Middle East often present with a high degree of microvascular and macrovascular complications at a relatively younger age compared with native Swedes [21,31], and that earlier age at diabetes onset is associated with poorer subsequent glycaemic control [17]. Consequently, we hypothesized that glycaemic control, as estimated by HbA1c, in this immigrant population with early diabetes onset would be worse than that of a population with later onset. Few studies have assessed long-term glycaemic control in ethnically diverse non-diabetic populations. Our data confirm that, in participants not previously diagnosed with diabetes, Iraqis do indeed have poorer glycaemic control than do Swedes. In addition, in this survey, almost 20% of FH++ individuals had HbA1c levels >42 mmol/mol, indicating a high risk of diabetes as proposed by recent studies [28].

To the best of our knowledge, this is the first study showing that ethnic differences in glycaemic control can be explained by an extended FH of diabetes rather than by other traditional risk factors such as age, gender, excess weight, larger waist circumference, T2D, physical inactivity and socioeconomic status.

Early detection of elevated levels of HbA1c indicates the need for intensive lifestyle interventions to prevent early disease onset [28]. The US National Diabetes Prevention Program has shown that lifestyle interventions are more efficient in preventing T2D than medication with metformin [32]. The programme is being conducted in a Western population with a low prevalence of diabetes FH. As our data suggest that glycaemic control in the non-diabetic stages is strongly influenced by family clustering, the present study highlights the need for preventative studies targeting individuals with family clustering of diabetes, with an emphasis on identifying the optimal medical and non-medical preventative actions against diabetes in this group. However, studies have revealed major challenges in addressing lifestyle changes in sedentary individuals with familial risks of diabetes [33]. Studies have also reported social and cultural obstacles to increased physical activity in Middle Eastern immigrant female populations [34]. Thus, prevention programmes targeting this high-risk group will also need to address these challenges to be successful [35,36].

4.4. Strengths and limitations

The major strengths of the present study are that it is population-based and represents a large proportion of the Iraqi population in the region matched with Swedish citizens living in the same geographical and socioeconomic neighbourhood. Our study is also distinct from other studies of this topic in that it includes OGTTs with repeated measurements, as well as detailed metabolic phenotyping and assessments of socioeconomic status and lifestyle factors. 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 ranges 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 [37]. Thus, when studying glycaemic control, only participants without previously diagnosed diabetes were included to avoid biasing the outcome of our data.

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

This population-based study of immigrants in Sweden from the Middle East contributes novel findings showing earlier diabetes onset and, in those without previously diagnosed diabetes, poorer glycaemic control compared with the native Swedish population. Furthermore, this study shows that an 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 assessed for diabetes using fairly broad screening criteria focused on a wide range of indications, especially those with a diabetes FH and/or obesity. We conclude that clinical interventions tailored to this high-risk group, particularly those with an extended FH of the disorder, may be an appropriate prioritisation of healthcare resources in Northern European countries.

6. Authors’ contributions

LB designed the study, wrote the research protocol, obtained, analysed 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 analysing the data and writing the manuscript. All authors have revised/edited the article critically and have approved the final version of the manuscript.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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Appendix A. Supplementary data

Supplementary materials (Fig. S1) and the French abstract associated with this article can be found at http://www.sciencedirect.com at http://dx.doi.org/10.1016/j.diabet.2014.08.003.

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