Diabetes mellitus in genetically isolated populations in Jordan: prevalence, awareness, glycemic control, and associated factors

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ABSTRACT

Objectives: Diabetes mellitus is one of the most common non-communicable diseases globally. This study seeks to estimate the prevalence of impaired fasting glycemia and type 2 diabetes mellitus in genetically isolated populations in Jordan: the Circassians and Chechans.

Research Design and Methods: Data were analyzed from a cross-sectional study that included a random sample of adult Circassians and Chechans. A subject was defined as affected by diabetes mellitus if diagnosis was known to patient or, according to the American Diabetes Association definition. Impaired fasting glucose was defined as a fasting serum glucose level of ≥ 6.1 mmol/L (100 mg/dl) but < 7 mmol/L. HbA1c > 7% was defined as ‘unsatisfactory’ metabolic control.

Results: The prevalence of impaired fasting glycemia was 18.5% for Circassians and 14.6% for Chechans. Prevalence of diabetes was 9.6% for Circassians and 10.1% for Chechans. The prevalence of impaired fasting glycemia and diabetes were significantly higher in men, older age groups, married, subjects of lower educational level, past smokers, and subjects with obesity. Low high-density lipoprotein cholesterol was the most common abnormality in the two populations.

Conclusions: The homogenous, genetically isolated Circassian and Chechan populations sharing the same environmental influences suggest a role for genetic risk factors for diabetes. Thus these two populations are suitable for additional genetics studies that may lead to the identification of novel risk factors for type 2 diabetes. In addition, more than half of patients with diabetes were with unsatisfactory control. Therefore, they are likely to benefit from programs encouraging healthy weight and physical activity.

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1. Introduction

Type 2 diabetes is characterized by defects in both insulin secretion and insulin action (Zimmet et al., 2001). The long-term effects of diabetes are severe including cardiovascular disease, retinopathy, nephropathy and neuropathy (Stumvoll et al., 2005). Diabetes is a genetically complex disease in which genetic variants predispose individuals to develop the disease. However, environmental factors play a major role in the development of the disease as the rapid rise of diabetes prevalence over the last few decades suggests (Zimmet et al., 2001). Epidemiological studies in different populations around the world have shown variation in the prevalence of diabetes among different ethnic groups (Jamil et al., 2009; Ujic-Voortman et al., 2009). The population in Jordan is comprised of three main ethnicities: Arab, Circassian and Chechan. The Arabs are the original inhabitants of Jordan while the Circassians and Chechans migrated to Jordan 140 years ago from their original countries, Cacas, and Chechnya, respectively. Within their countries, these populations were genetically, geographically, and culturally isolated (Barbujani, Nasidze et al., 1994; Bulayeva, 2006; Kailani, 2002; Nasidze et al., 2004; Richmond, 2008). They settled in Amman, the capital of Jordan and the surrounding area. According to unofficial estimates, the Circassian population varies from 60,000 to 80,000 individuals (Richmond, 2008), and the Chechan population is around 10,000 individuals (Kailani, 2002).

Both Circassians and Chechans in Jordan have managed to maintain their identity and ethnicity during the last 100 years. One
of the main ways they have done this has been through endogamous marriages, the use of the original language and the preservation of certain traditions of their respective cultures. A recent study showed that the prevalence of diabetes in Jordan is 17.1% (Ajlouni et al., 2008). There are no studies on the prevalence of diabetes in the Circassian and Chechan population in Jordan. There is only one study on the Circassian population in Israel (Haron et al., 2006). Studying these genetically isolated populations is very important to provide a baseline for future genome wide association studies on these populations to discover novel risk factors associated with diabetes (Elbein, 2009).

The objective of this study was to estimate the prevalence of impaired fasting glycemia (IFG) and type 2 diabetes mellitus (DM), assess the awareness and glycemic control of diabetes, determine factors associated with diabetes and determine the metabolic disorders associated with diabetes in the Circassian and Chechan populations in Jordan.

2. Research design and methods

2.1. Study population and data collection

This study has been approved by the institutional review board committee at the Center for Diabetes, Endocrinology and Genetics. A survey was conducted in six areas where Circassians and Chechans cluster, namely, Wadi El-seer, Swielh and Jerash, were chosen to study Circassians and Zarqa, Sukneh and Swielh were chosen to study Chechans. A team of two visited all the households in each area. They invited the residents to attend the community center at a set date after an overnight fast and explained the purpose of the study. Subjects on regular medications were asked not to take their medications early at that day and to bring all their medications with them to the survey site. To encourage participation, community and religious leaders and the municipality were contacted to secure subjects' co-operation. The study team worked in all week days including weekends to encourage employed people to participate. Participants attended the community centre with a minimum fasting time of 8 hours. A pilot-tested structured questionnaire prepared specifically for the study was administered by trained interviewers to collect information on socio-demographic factors, DM, hypertension, hyperlipidemia, smoking habits, and potential risk factors. Data were collected in the period between August 2008 and March 2009. All subjects provided written informed consent to the investigation. To ensure that all we sampled were pure Circassians/Chechans, each participant in the study filled out a survey that included pedigree information. The names and ethnicity of parents, grandparents, great grand parents both maternal and paternal and any individual with non Circassian/Chechan heritage for even one person in his/her pedigree was excluded.

2.2. Measurements and laboratory analysis

Anthropometric measurements including weight, height, hip and waist circumferences, were measured with the subjects wearing light clothing and no shoes. Waist circumference was measured to the nearest centimeter using non-stretchable tailor’s measuring tape at the midway between the lower rib margin and the iliac crest. The hip circumference was measured at the widest part of the body below the waist. Body mass index (BMI) was calculated. Two readings of systolic and diastolic blood pressure were taken from the left arm with the subject seated and the arm at heart level, using standardized mercury sphygmomanometer. The mean of the two readings were taken as the individual’s blood pressure. For laboratory analysis and all biochemical measurements, two sets of fasting blood samples were drawn from a cannula inserted into the antecubital vein into sodium fluoride potassium oxalate tubes for glucose and lithium heparin vacuum tubes for lipids. Samples were centrifuged at 3000 rpm for 10 minutes within 1 hour at the survey site, and plasma was transferred to separate labeled tubes and transferred immediately in cold boxes filled with ice to the central laboratory of the National Center for Diabetes and Endocrinology. Lipid parameters [total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triacylglycerol], and glucose were analyzed for all samples using enzymatic assays.Glucose level was determined using the enzymatic reference method with hexokinase. Triacylglycerol values were obtained on COBAS INTEGRA 700 with the cassette COBAS INTEGRA Triacylglycerol using enzymatic, colorimetric method (GPO/PAP) with glycerol phosphate oxidase and 4-aminophenol. Total cholesterol was analyzed using enzymatic, colorimetric method with COBAS INTEGRA Cholesterol Gen.2. HDL cholesterol and LDL cholesterol values were obtained on COBAS INTEGRA 700 using homogeneous enzymatic colorimetric assay. The assays were conducted according to the manufacturers’ instructions.

2.3. Definition of variables

Participants were assessed for previously diagnosed diseases using the question: “Have you ever been told by a doctor or health professional that you have that disease?” Those who answered “yes” to this question were defined as having previously diagnosed disease. Age at diagnosis for those patients was determined using the question: “When a health professional first told you that you had that disease?” A subject was defined as affected by diabetes mellitus if this diagnosis is known to the patient or, according to the American Diabetes Association (ADA) definitions, if fasting serum glucose is 7 mmol/l (126 mg/dl) or more. Impaired fasting glucose was defined as a fasting serum glucose level of ≥6.1 mmol/l (100 mg/dl) but <7 mmol/l. The glycemic control was assessed using HbA1c. Patients with previously diagnosed diabetes who had HbA1c ≥7% were defined as having ‘unsatisfactory’ glycemic control. A family history of diabetes mellitus was self reported by participants and defined as positive if at least one first or second degree relative had diabetes mellitus. Obesity was defined as having a BMI ≥30, as defined by the World Health Organization (WHO). Other metabolic abnormalities were defined according to the National Cholesterol Education Program’s Adult Treatment Panel III report (ATP III) criteria for the metabolic syndrome (2002) as follows:

- Abdominal obesity: waist circumference >102 cm (40 in) in men and ≥88 cm (35 in) in women.
- High blood pressure: systolic blood pressure ≥130 and/or diastolic blood pressure ≥85 mmHg or on treatment for hypertension.
- Hypertriglyceridemia: serum triglycerides level ≥150 mg/dl (1.69 mmol/l).
- Low HDL cholesterol: serum HDL cholesterol <40 mg/dl (1.04 mmol/l) in men and <50 mg/dl (1.29 mmol/l) in women.

2.4. Statistical analysis

Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS version 15). Data were described using mean and standard deviation for continuous variables and proportions for categorical variables. Chi-square test was used to compare proportions. Multivariate logistic regression was used to assess the factors associated with impaired fasting glucose and diabetes mellitus among Circassians and Chechans. A P-value of less than 0.05 was considered statistically significant.
3. Results

3.1. Participants’ characteristics

The study included 437 Circassians (160 males and 277 females) and 355 Chechans (119 males and 236 females) aged 18 years and above. The response rate was 80% among Circassians and 80% among Chechans. The mean (SD) age was 43.0 (15.5) year for Circassians and 45.4 (16.8) for Chechans. The prevalence of IFG and diabetes did not differ between Circassians and Chechans. Circassians had higher level of education compared to Chechans. The prevalence of low HDL was higher in men, older age groups, married, subjects of lower educational level, past smokers, and subjects with obesity.

3.2. The prevalence of IFG and DM

The prevalence of IFG was 18.5% for Circassians and 14.6% for Chechans and prevalence of diabetes was 9.6% for Circassians and 10.1% for Chechans. The prevalence of IFG and diabetes did not differ significantly between Circassians and Chechans. Both racial groups had similar distribution of IFG and diabetes according to important variables. Therefore, Table 2 shows the prevalence of IFG and diabetes according to relevant characteristics for Circassians and Chechans combined. The prevalence of IFG and diabetes were significantly higher in men, older age groups, married, subjects of lower educational level, past smokers, and subjects with obesity.

3.3. Awareness of diabetes and glycemic control

Of the total patients with diabetes, 69.0% of Circassians and 86.1% of Chechans with diabetes had been previously diagnosed and the rest were detected by the study. More than two thirds of previously diagnosed (79.3% for Circassians and 71.0% for Chechans) were on regular diabetes medications. About two thirds of patients in both groups reported that they were on diet. Of the previously diagnosed cases, 33.3% of Circassians and 16% of Chechans reported regular monitoring of blood sugar at least once daily and 23.8% of Circassians and 50.0% of Chechans reported regular visits to the internist. Of the previously diagnosed, 44.8% of Circassians and 61.3% of Chechans were found to be under unsatisfactory glycemic control (HbA1c < 7.0%).

About 4% of patients in both groups reported that they attended emergency clinics for diabetes reasons and 8.7% of Circassians and 4% of Chechans reported that they were hospitalized because of their diabetes.

3.4. Factors associated with IFG and DM

Table 3 shows the multivariate analysis of factors associated with IFG and DM. Increase in age, central obesity, and male gender were
significantly associated with increased odds of IFG and DM. After adjusting for significant variables in the model, there were no significant differences between Circassians and Chechans in the odds of IFG (P-value = 0.076) and diabetes (P-value = 0.746).

### 3.5. IFG, DM and other metabolic disorders

Overall, 18.5% of Circassians and 30.4% of Chechans had hypertension and 42.3% of Circassians and 45.9% of Chechans had elevated triglycerides level. Low HDL cholesterol was the most common abnormality in the two populations (48.3% in Circassians and 66.8% in Chechans). Elevated triglycerides, low HDL cholesterol, and high blood pressure were more prevalent among patients with diabetes and patients with IFG compared to those with normal glucose level in Circassians and Chechans Table 4.

### 4. Discussion

This is the first study to report the prevalence of diabetes in the Circassian and Chechan population in Jordan. This report is also the first for the Chechan population anywhere in the world and the only second study on the Circassian population anywhere in the world.

The prevalence of impaired fasting glycemia was 18.5% for Circassians and 14.6% for Chechans. Prevalence of diabetes was 9.6% for Circassians and 10.1% for Chechans.

Our data showed that the prevalence of DM in the Circassian and Chechan population is similar. There were no significant differences in sociodemographic, anthropometric and clinical characteristics between the two groups. The prevalence of diabetes in the Circassian population in Israel has been reported to be 12% (Haron et al., 2006) which is higher than what we reported. The WHO and ADA have revised the criteria for diagnosing diabetes (Committee, 2003). Age- and sex-specific prevalence of diabetes according to the WHO and ADA criteria are not widely available. Comparing prevalence rates from other studies is not accurate because of the use of different criteria for diagnosis, different cut off points and different age groups studies. Nevertheless, A recent report from Jordan reported a much higher prevalence rate (17%) (Ajlouni et al., 2008) compared to the rates in the Circassian and Chechan populations. This is an increase in the prevalence rate reported in Jordan 1994 of 13% (Ajlouni et al., 1998). This suggests that the ethnicity of these populations may play a role in the predisposition to diabetes onset since all populations share similar environments.

The age standardized prevalence of diabetes in the Circassians and Chechans is higher than that reported in Chinese adult population (Gu et al., 2003) and rural population of Bangladesh (Sayeed et al., 2003) but similar to that reported in Spain (Masia et al., 2004).

The age standardized prevalence of IFG is higher than reported in a number of studies (Gu et al., 2003; Masia et al., 2004; Sayeed et al., 2003). There has been an increase in prevalence of diabetes in some Gulf countries including Saudi Arabia (Al-Nuaim, 1997), United Arab Emirates (el Mugamer et al., 1995), and Oman (Al-Lawati et al., 2002).

The variation of prevalence between areas can be understood as reflecting environmental and/or genetic variations in the population. A higher prevalence can reflect factors such as adoption of a sedentary lifestyle, characterized by changes in dietary habits and reduction in physical activity, and the resulting obesity. However, high prevalence of diabetes does not necessarily indicate high incidence, because high prevalence may reflect better case ascertainment and prolonged survival of diabetic patients as suggested by the findings of others (Berger et al., 1999).

The prevalence of IFG and diabetes were significantly higher in men, older age groups, married, subjects of lower educational level, past smokers, and subjects with obesity. A high percentage of diabetics from both populations had been previously diagnosed reflecting a high level of awareness of the disease in these populations. This rate is higher than that reported from many developing countries (McLarty et al., 1989) and some developed countries (Andersson et al., 1993; Wandell et al., 1998). A number of studies have reported that patients with undiagnosed diabetes represent 25% to 66% of the overall diabetic population (Glumer et al., 2003; Wilks et al., 1999). However, much lower figures of undiagnosed diabetes were reported from countries such as Sudan (1%) (Abdelgadir et al., 2006) and the United States (4.3 and 6.3%) (Harris et al., 1998).

Despite the high awareness of diabetes (Andersson et al., 1993), a high proportion of patients with previously diagnosed diabetes still have unsatisfactory metabolic control.

More than two thirds of previously diagnosed patients were on regular diabetes medications. About two thirds of patients in both groups reported that they were on diet. Of the previously diagnosed cases, 33.3% of Circassians and 16% of Chechans reported regular monitoring of blood sugar at least once daily and 23.8% of Circassians and 50.0% of Chechans reported regular visits to the internist. These numbers indicate that treatment was not effective or there is a lack of compliance with the treatment protocol. It is possible that patients rely much on medications and ignore the need to modify their eating habits and increase physical activity. Another possibility is a conservative attitude of attending physicians where they attempt to keep glycemic levels above that recommended for fear of hypoglycemia.

Diabetes was significantly related to increase in age, central obesity and male gender and prevalence was higher among those with the least education in both populations.

### Table 3

<table>
<thead>
<tr>
<th>Racial group</th>
<th>Impaired fasting glycemia</th>
<th>Diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% confidence interval)</td>
<td>P-value</td>
</tr>
<tr>
<td>Circassian</td>
<td>1.45 (0.96, 2.17)</td>
<td>.076</td>
</tr>
<tr>
<td>Chechan</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4

<table>
<thead>
<tr>
<th>Racial group</th>
<th>Hypertension</th>
<th>Elevated triglycerides</th>
<th>Low HDL-c</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Circassian</td>
<td>314</td>
<td>42 (13.4)</td>
<td>106 (33.8)</td>
</tr>
<tr>
<td>Normal</td>
<td>106 (33.8)</td>
<td>134 (42.7)</td>
<td></td>
</tr>
<tr>
<td>Impaired fasting glycemia</td>
<td>81 (40.3)</td>
<td>106 (33.8)</td>
<td>56 (27.8)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>42 (20.7)</td>
<td>134 (42.7)</td>
<td>56 (27.8)</td>
</tr>
<tr>
<td>Chechan</td>
<td>267</td>
<td>60 (22.5)</td>
<td>100 (37.5)</td>
</tr>
<tr>
<td>Normal</td>
<td>267</td>
<td>167 (62.5)</td>
<td></td>
</tr>
<tr>
<td>Impaired fasting glycemia</td>
<td>52 (24.6)</td>
<td>167 (62.5)</td>
<td>35 (67.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>36 (16.9)</td>
<td>41 (78.3)</td>
<td>41 (78.3)</td>
</tr>
</tbody>
</table>
Low HDL cholesterol was the most common abnormality in the two populations. Elevated triglycerides, low HDL cholesterol and high blood pressure were more prevalent among patients with diabetes and patients with IFF compared to those with normal glucose level in Circassians and Chechans. The prevalence of low HDL was higher in Chechans compared to Circassians. Several studies, performed in elderly men or in populations with a high incidence of DM, have observed that elevated blood pressure, elevated serum concentrations of total and low LDL cholesterol, low HDL cholesterol and triglycerides predict the future occurrence of DM. However, because of the important role of insulin resistance in the pathogenesis of DM and these cardiovascular risk factors, these components of the metabolic syndrome may be confused with overweight and glucose intolerance (Davies, 1999). It is therefore not clear whether they are independent risk factors.

One limitation of this study is that several well-known factors that can have impact on diabetes like diet and physical activity were not examined. Previous studies, which compared the WHO and ADA criteria, showed various degrees of concordance with respect to diagnosis of manifest DM and great discordance with respect to diagnosis of the prediabetic state (Harris et al., 1997). Moreover, compared to impaired glucose tolerance (WHO), impaired fasting glucose (ADA) had a weaker association with cardiovascular morbidity and all-cause mortality (Barzilay et al., 1999). This suggests that the ADA criteria may underestimate the burden of glucose disorders (Davies, 1999).

The present survey was conducted in genetically isolated populations that are relatively well defined, stable, and accessible. These characteristics facilitate future follow up studies using the same sample. Such studies may provide useful information on the incidence of diabetes, the rate of progress from prediabetic to diabetic state, changes in diabetes control, as well as the prognosis of diabetic patients.

This study also sets a baseline for these two ethnic populations. It would be interesting to study the changes in rates over time to see if it mimics the Jordanian population or not since they share the same environment. Such studies will give an indication of the role of heredity in the prevalence of diabetes and provides a unique opportunity to study the effect of the environment and behaviors on the prevalence of diabetes.

In addition, studying these genetically isolated populations will set the stage for genome wide association studies on these populations to discover novel risk factors associated diabetes (Hirschhorn & Daly, 2005). Based on the predictions from population genetic theory it is expected that isolated populations such as the Circassian and Chechan populations in Jordan that have gone through severe bottlenecks or which have remained at a constant small size for a long time to have extensive linkage disequilibrium such as the Circassian and Chechan populations in Jordan that have population genetic theory it is expected that isolated populations will give an indication of the role of insulin resistance in the pathogenesis of DM and these cardiovascular risk factors, these components of the metabolic syndrome may be confused with overweight and glucose intolerance (Davies, 1999). It is therefore not clear whether they are independent risk factors.

References


