Incidence of diabetic eye disease among migrants: A cohort study of 100,000 adults with diabetes in Denmark

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ABSTRACT

Aims: To examine the incidence rates of any and referable diabetic retinopathy (DR) among migrants in Denmark.

Methods: Nationwide clinical data on diabetes patients followed since 2005 were analysed. Patients were classified according to country of origin into six groups: Denmark, other Europe, Sub Saharan Africa, Middle East/North Africa, Asia, and America/Oceania. A total of 93,780 or 110,897 patients without any (including unspecific diagnoses) or referable (proliferative) DR at baseline were analyzed. We estimated event rates and hazard ratios (HRs) for incidence of any and referable DR according to country of origin.

Results: After an average follow-up of 3.59 years 6727 had incident any DR and 4747 patients had referable DR. Compared to people of Danish origin, migrants from the Middle East/North Africa and Asia had a higher risk of any and referable DR after adjustment for age, sex, body mass index, smoking status, types and duration of diabetes, clinic type (general practice vs outpatient clinic), HbA1c, blood pressure and lipid levels. The associations remained significant after further adjustment for frequency of eye screening.

Conclusions: Migrants from the Middle East/North Africa and Asia were at increased risk of developing any and referable DR compared to native Danes, and these differences were not fully explained by differences in underlying clinical, diabetic and cardiometabolic risk factors.

1. Introduction

Global migration is increasing and 232 million people, or 3.2 percent of the world's population were international migrants in 2013 compared with 175 million in 2000 [1]. In Denmark, migrants constitute about 10% of the total population and two thirds of migrants originate from a non-Western country [2]. It has been reported that migrants from non-European countries are diagnosed with diabetes more commonly and at a younger age than European counterparts [3–5]. Consequently, they may have higher rates of diabetic complications. Diabetic retinopathy (DR) is a common microvascular complication of diabetes and may progress to proliferative retinopathy and macular oedema if exposure to hyperglycemia and hypertension prolongs. Cross sectional studies from UK and US have shown that African, Hispanic and South Asian

migrants with diabetes have a higher prevalence of DR and especially sight-threatening retinopathy, than UK and US born people with diabetes [6–8]. It has been considered that this difference reflects worse glycemic and blood pressure (BP) control, longer diabetes duration, lower frequency of eye examination and genetic background [7,9]. Although the prevalence of DR has been decreasing in US and visual impairment by DR may be decreasing in UK owing to DR surveillance programs and improvement of diabetes care [10,11], nationwide longitudinal data on incidence of DR among migrants are lacking. Therefore, the aim of this study is to investigate the incidence of any DR and referable DR among migrants in Denmark; secondly to study whether such differences are explained by differences in underlying risk factors.

2. Methods

2.1. Patient population

Information on diabetes treatment status and levels of intermediate clinical measures was obtained from the Danish Adult Diabetes Registry (DADR) [12]. Since 2005, all diabetes outpatient clinics in Denmark are obliged to report clinical data yearly to DADR, whereas reporting from the general practitioners was included on a voluntary basis from 2006. Reporting is done either as manual data entry from paper records or through automated data capture systems from electronic patient records. Thus, for more than 90% of the patients treated at Danish outpatient clinics, DADR contains annual assessments of a range of clinical markers, anthropometry, lifestyle related factors, treatment, and results of complications screening performed between 2005 and 2013. Since reporting from general practitioners was gradually added from 2006, there is a lower coverage among this patient population.

Through the unique personal identification number given to all Danish residents at birth and recorded in the Danish Civil Registration System [13], data from DADR was linked with morbidity data (ICD-10 codes) from the Danish National Patient Register [14]. This linkage allowed individual level information on dates and diagnoses related to DR. Information on date and cause of death was obtained through linkage to the Cause of Death Register [15] and information on country of birth was obtained from the Central Personal Register.

From a total of 129,042 persons registered with a unique personal identification number in DADR, we excluded 4836 with missing information on region of origin, diabetes type, age and sex. In analyses of incident any DR, 30,426 patients with prevalent any DR at baseline were excluded leaving 93,780 in the analyses. Similarly, 13,313 patients with prevalent referable DR at baseline were excluded from analyses of incident referable DR, leaving 110,897 patients for analyses. Further, in multiple adjusted models we excluded patients with missing data of any baseline anthropometry or laboratory measurement, leaving 47,699 and 60,492 patients for analyses in the fully adjusted models of any and referable DR, respectively. A flow chart of the data included in analyses is presented in Fig. 1.

2.2. Measurements

Annual measurements reported to DADR from outpatient clinics and general practitioners included height, weight, BP and results of a number of laboratory tests of collected blood samples. These comprise HbA1c, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and triglyceride. Other data collected in DADR included diabetes type, smoking status, alcohol intake, self-reported exercise, antihypertensive medication use, lipid-lowering medication use in addition to date and results of screening for complications including eye-screening. Smoking status is self-reported and was classified into four categories (never, past, occasionally and current smoker). We classified patients according to country of origin into six groups: Denmark, other Europe, Sub Saharan Africa, Middle East/North Africa, Asia and America/Oceania.

In Denmark, treatment requiring DR is referred to ophthalmological specialist units, and reporting of diagnostic codes and procedures to the National Patient Register is therefore mandatory, whereas simplex retinopathy is not systematically registered. We defined referable DR according to International Classification of Diseases ICD-10 as proliferative retinopathy including artificial eye, vascular endothelial growth factor treatment or retinal and corpus vitreum operations including laser procedure. To define any DR, unspecified diagnoses of retinopathy were included (e.g. ICD-10 codes E103, E113, E133, E143) in addition to the referable DR codes. Corresponding ICD-8 codes were used to identify events prior to 1995, and procedure-codes based on the Danish SKS-system [16] was used to identify surgery and other procedures that indicated any or referable DR. The specific ICD-10, ICD-8 and SKS procedure codes used in the definitions of any and referable DR are provided in the supplemental material (supplemental Table 1). In order to rule out the possibility that some diagnoses of retinopathy not related to diabetes were identified as DR, we performed sensitivity analyses leaving out retinopathy diagnoses that might occur independently of diabetes. These "strict" definitions are also shown in supplemental Table 1.

2.3. Statistical analysis

Statistical analyses were performed using R version 3.1.2 and Stata/IC, version 14.2. All reported p values are two-tailed, and $p < 0.05$ was considered statistically significant.

First, the equality of means of each variable at baseline was examined by region of origin and compared to people of Danish origin in linear regression models. The chi-squared test was used to compare the proportions. Incidence rates (IR) for any and referable DR were calculated by region and hazard ratios (HR) were used to compared to people of Danish origin after adjusting for confounding factors. In a crude model (model 1), we adjusted for age, sex and diabetes type. In a second model (model 2), we additionally adjusted for body mass index (BMI), smoking status, duration of diabetes, HbA1c, clinic type (general practice vs outpatient clinic), BP and lipids. Then, in a final model (model 3) we