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Risk factors for diabetic retinopathy in people with Type 2 diabetes: A case–control study in a UK primary care setting

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ABSTRACT

Aim: To identify risk factors of diabetic retinopathy (DR) among people with Type 2 diabetes mellitus in UK primary care.

Methods: A case–control study nested in a cohort of incident Type 2 diabetes identified in The Health Improvement Network database from 2000 to 2007. Cases were people with DR ($N = 7735$) and controls were a DR-free sample ($N = 9395$). No age restrictions were applied. Adjusted odds ratios and 95% CIs were estimated.

Results: 21% of DR cases were identified during the first semester after Type 2 diabetes diagnosis. After controlling for delay on the Type 2 diabetes diagnosis, the DR risk increased with the duration of diabetes. DR increased with a mean systolic BP ≥150 mmHg (1.18; 1.10–1.27), high alcohol consumption (1.34; 1.11–1.61), glycated haemoglobin (≥75 to <86: 1.14; 1.00–1.31; ≥86 to <97 mmol/mol: 1.25; 1.07–1.45; ≥97 mmol/mol: 1.21; 1.07–1.37), microalbuminuria (1.16; 1.06–1.27), and retinal vein occlusion (2.47; 1.67–3.66). Glaucoma and retinal arterial occlusion showed an OR of 0.71 (0.60–0.84) and 0.63 (0.40–1.01), respectively. HDL ≥1.55 mmol/l (0.88; 0.80–0.98), high triglycerides (2.3–5.6 mmol/l: 0.90; 0.82–0.99; >5.6 mmol/l: 0.85; 0.64–1.13) or smoking (0.89; 0.81–0.97) had a slightly reduced DR risk. Users of hypoglycaemic agents had an increased DR risk.

Conclusion: Some DR cases were identified near the diabetes diagnosis date suggesting that a delayed diabetes diagnosis is still common. Glaucoma, retinal arterial occlusion and high HDL levels were inversely associated with DR, while retinal vein occlusion, alcohol and other well-known risk factors were positively associated.

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1. Introduction

People with diabetes are at an increased risk for a wide range of comorbidities and complications. Among them, diabetic retinopathy (DR) remains a leading cause of blindness in the working-age population in the United Kingdom (UK) [1] and other developed countries [2]. Several physiopathological pathways have been proposed in the pathogenesis of DR [3]. Notably, chronic retinal hypoxia and progressive retinal ischaemia have been shown to trigger the development of DR [4]. Although poor glycaemic control is a known determinant of DR [5], other modifiable factors are likely to play a role in its pathogenesis and should be identified.

The aim of this study was to identify risk factors associated with the development of DR among people with Type 2 diabetes mellitus managed in a primary care setting in the UK.

2. Materials and methods

2.1. Data source

The Health Improvement Network (THIN) is a longitudinal primary care medical records database containing anonymized data on over 3 million active people currently registered with participating UK primary care practices [6]. These people are representative of the entire UK population with respect to age, sex and geographical region [7]. The THIN database contains individual patient demographic and clinical information recorded by primary care practitioners (PCPs) as part of their routine clinical care, such as PCP consultations, referrals, hospitalizations, laboratory test results and prescriptions issued by PCPs. Letters from specialist visits and hospital admissions (i.e. discharge letters) are also available. Diagnoses and test procedures are recorded using Read codes [8]. Prescriptions written by PCPs are generated and recorded automatically in the database using a coded drug dictionary (Multilex) [9]. The study protocol was approved by the UK Research Ethics Committee (09/H0305/64).

2.2. Study cohort and case ascertainment

A case–control study nested in a cohort of people with Type 2 diabetes was performed. Detailed information on the study cohort has been published elsewhere [10,11]. Briefly, the study cohort was composed of all people newly diagnosed with Type 2 diabetes from January 2000 to December 2007 who were free of any diagnosis code for retinopathy or maculopathy, whether diabetes related or unspecified, recorded any time before or on the same date of the first diagnosis of diabetes ($N = 63{,}226$). No age restrictions were applied. Newly diagnosed diabetes was defined as the first recorded diabetes diagnosis through READ code or the first recorded antidiabetic treatment whichever came first during each patient time recorded in THIN. The diabetes onset was the date of new that record. People with incident Type 2 diabetes were followed from onset until the first recorded READ code suggesting an incident diagnosis of retinopathy related to diabetes from 2000 to 2008 [11]. List of READ codes used to identify DR has been published elsewhere [10]. The date of DR was the index date for the case–control analysis. A random sample of DR diagnoses were validated in a two-step procedure including a manual review of the computerized patient profiles after incorporating free-text comments and responses to questionnaires sent to PCPs. The confirmation rate of the diagnosis of DR and its incident date was 78.0% for the entire sample of the computer-detected DR participants [10]. All DR detected through computer in the incident Type 2 diabetes cohort, but those not confirmed by general practitioners, were included in the current risk factors assessment evaluation.

2.3. Control selection

People with Type 2 diabetes without DR constituted the pool of participants for control selection. A date during the study period was generated at random for each of the potential controls. If the random date was included in his/her follow-up period, that person was marked as an eligible control and the random date was used as index date. We randomly selected 9395 controls.

2.4. Risk factors assessment

The following information on potential risk factors was derived from the THIN database:

1. Demographic and lifestyle factors: age, sex, body mass index (BMI, kg/m^2), smoking status and alcohol consumption (units per week; 1 unit of alcohol is equal to 10 mL (~8 g) ethanol), according to the most recent status before the diabetes onset.
2. Healthcare service use: number of PCP visits, referrals and hospitalizations, from one year before to 15 days before the index date.
3. Relevant laboratory test results between the onset of diabetes and the index date: glycated haemoglobin (HbA1c, mmol/mol, (%), the first value after diabetes diagnosis and the mean value of all available measurements), systolic and diastolic blood pressure (BP, mmHg, the last value before the index date and the mean value of all available measurements), microalbuminuria (defined as having a recorded value of urine albumin of 30–300 mg/L or 3–30 mg/mmol of creatinine), proteinuria (defined as having a recorded value of urine albumin of 300–30,000 mg/L or >30 mg/mmol of creatinine), and lipid levels (including total cholesterol, LDL, HDL and triglycerides, in mmol/l, the last values before the index date).
4. Prior history of other diseases, including ocular and cardiovascular diseases, was collected: glaucoma, retinal arterial occlusion, retinal vein occlusion, cataracts or lens extraction, myopia, hypertension, hyperlipidemia, ischaemic heart disease (IHD) and heart failure (HF).
5. Exposure to hypoglycaemic agents and drugs used for cardiovascular diseases was ascertained prior to the index date and classified into 3 mutually exclusive time windows: (1) current use, when the most recent prescription lasted until the index date or ended in the 30 days prior to the index date; (2) recent use, when use ended between 31 and 365 days prior to the index date; and (3) non-use, when