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Prevalence and risk factors for diabetic retinopathy in Asian Indians with young onset Type 1 and Type 2 Diabetes

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ABSTRACT

Aim: To assess the prevalence and risk factors for diabetic retinopathy (DR) in people with young onset type 1 (T1DM-Y) and type 2 diabetes (T2DM-Y).
Methods: T1DM-Y(n = 150) and T2DM-Y(n = 150) participants, age between 10 and 25 years at diagnosis, had a complete clinical evaluation, biochemical assessment, and four field digital retinal colour photography. The Early Treatment Diabetic Retinopathy Study grading system was used to grade DR. Proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) were considered as sight threatening DR.
Results: The prevalence of any DR was 53.3% [95% CI 45.3–61.3] in T1DM-Y (duration of diabetes: 12.4 ± 7.4years) and 52.7% [44.7–60.7] in T2DM-Y (11.8 ± 8.3 years). The age and gender adjusted prevalence of DR, DME and PDR was 62.5%, 10% and 7.3% in T1DM-Y, whereas it was 65.8%,12.7% and 9.3% in T2DM-Y respectively. In multivariable logistic regression, diabetes duration [Odds ratio (OR) 1.99 per 5 years; CI 1.42–2.79], waist circumference [1.28 per 5 cm;1.05–1.56] and microalbuminuria [2.39 per 50 μg;1.07–5.31] were associated with DR in T1DM-Y, and diabetes duration [2.21 per 5 years; 1.61–3.02], diastolic blood pressure [1.54 per 5 mmHg;1.18–2.02], Glycated hemoglobin [1.37 per %;1.07–1.75] and lower stimulated C-peptide [1.54 per 0.5 pmol/ml;1.15–2.05;] were associated with DR in T2DM-Y.
Conclusion: Over half of the people with young-onset diabetes, regardless of type, have retinopathy within 10–12 years of diabetes duration, emphasizing the need for regular eye screening and aggressive control of glucose and blood pressure to prevent DR.

1. Introduction

The growing burden of diabetes globally has been accompanied by a rise in numbers of young onset type 1diabetes (T1DM-Y) and particularly young onset type 2 diabetes (T2DM-Y) (American Diabetes Association, 2000; Amutha et al., 2011; International Diabetes Federation, 2011; McMahon et al., 2004; Mohan, Jaydip, & Deepa, 2007; Pinhas-Hamiel & Zeitler, 2005). Younger age of onset of diabetes results in a longer life time exposure to hyperglycemia and consequently a greater risk of developing complications during productive years of adulthood (Amutha, Datta, Unnikrishnan, Anjana, & Mohan, 2012; Amutha et al., 2011; Hillier & Pedula, 2003; Pinhas-Hamiel & Zeitler, 2007).

Diabetic retinopathy (DR) is a potentially sight-threatening microvascular complication of diabetes, and an important cause of preventable blindness. While disease duration and levels of glucose and blood pressure control strongly influence the risk of DR (Chaturvedi et al., 1998; Klein, Klein, Moss, Davis, & DeMets, 1984a; Raman et al., 2009; Rema et al., 2005; The DCCT Research Group, 1993), some data indicate that younger age of onset, especially for T2DM, may confer added susceptibility to DR (Eppens et al., 2006; Wong, Molyneaux, Constantino, Twigg, & Yue, 2008). In the multi-ethnic SEARCH study in the US, the prevalence of DR was 17% in T1DM and 42% in T2DM (Mayer-Davis et al., 2012). Although diabetes in the young (particularly T2DM) is becoming more frequent in India (Amutha et al., 2011; Mohan et al., 2007), epidemiological data on DR in India are largely limited to adult onset T2DM (Raman et al., 2009; Rema et al., 2005), and to a few studies in T1DM-Y (Rema, Mohan, & Ponnaiya, 1995; Rema, Mohan, Ramachandran, & Viswanathan, 1989). Data in people with T2DM-Y are scarce.

Conflict of interest: None declared.

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We assessed the prevalence and risk factors for retinopathy in people with T1DM-Y and T2DM-Y, with onset of diabetes between ages 10 and 25 years, in a clinic population in India.

2. Research design and methods

Data for this study were collected between January 2010 and June 2011 from individuals with T1DM-Y (n = 150) and T2DM-Y (n = 150), diagnosed between the ages of 10 and 25 years, with duration of diabetes over 2 years, registered at Dr. Mohan's Diabetes Specialties Centre (DMDSC),a tertiary care network in Chennai (formerly Madras) in southern India. The Institutional Ethics Committee (IEC) approval was obtained prior to the start of the study. Written informed consent was obtained according to the local IEC guidelines and assent was obtained from the study subjects less than 18 years of age in addition to parental consent.

Diabetes was defined as fasting plasma glucose (FPG) level ≥126 mg/dl (7.0 mmol/l) and/or 2-h post-load glucose level ≥200 mg/dl (11.1 mmol/l) (Alberti & Zimmet, 1998) or self-reported diabetes treated by a physician or on hypoglycemic medications or insulin. Diabetes was then classified as follows: T1DM-Y, if accompanied by abrupt onset of symptoms like polyuria, polydipsia, or unexplained weight loss, diabetic ketoacidosis (DKA), absent insulin reserve as shown by fasting and stimulated C-peptide (<0.3pmol/ml), and requirement of insulin from the time of diagnosis for control of hyperglycemia; and T2DM-Y, as absence of ketosis, good beta cell functional reserve as evidenced by stimulated C-peptide (≥0.6 pmol/ml), absence of pancreatic calculi (on X-ray abdomen), and good response to oral hypoglycemic agents for more than 2 years (Amutha et al., 2011).

Anthropometric measurements included height, weight, and waist circumference (Deepa et al., 2003). Height was measured in centimetres using a stadiometer. Weight was measured with a traditional spring balance and recorded to the nearest 0.5 kg. Body mass index (BMI) was calculated using the formula: weight (kg)/height squared (in m^2). Waist circumference was measured using a non-stretchable measuring tape. The participants were asked to stand erect in a relaxed position with both feet together on a flat surface; one layer of clothing was accepted. Waist girth was measured as the smallest horizontal girth between the costal margins and the iliac crests at minimal respiration. Blood pressure was recorded in a rested sitting position in the right arm with a mercury sphygmomanometer and rounded off to the nearest 2 mmHg. Two readings were taken 5 min apart and the mean of the 2 readings was used.

Fasting plasma glucose (hexokinase method) was measured on Hitachi 912 Autoanalyzer (Hitachi, Mannheim, Germany) using kits supplied by Roche Diagnostics (Mannheim, Germany); glycated haemoglobin (HbA1C) by high-pressure liquid chromatography using the Variant machine (Bio-Rad, Hercules, Calif., USA); serum total cholesterol (cholesterol oxidase-peroxidase-amidopyrine method), serum triglycerides (glycerol phosphate oxidase-peroxidase-amidopyrine method), and HDL cholesterol (direct method-polyethylene glycol-pretreated enzymes) using Hitachi-912 Autoanalyser (Hitachi, Mannheim, Germany). Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald formula (Friedewald, Levy, & Fredrickson, 1972). Apo lipo-protein A and B were measured by immuno-turbidometric method (Olympus AU 2700 USA).

Fasting and stimulated (post-breakfast) C-peptide was estimated by the electro-luminescence method on Elecsys2010 (Hitachi, Mannheim, Germany); glutamic acid decarboxylase (GAD) antibodies were measured on a Bio-Rad plate reader 680 (USA) using Elisa Euro Immun kit (Lubeck, Germany); and plasma concentration of hs-CRP by turbidometry method (Beckman Coulter AU 480 USA). The intra- and inter-assay co-efficient of variation for the biochemical assays ranged between 3.1% and 7.6%.

Urine samples were collected after an overnight fast. Microalbumin concentration was measured using an immunoturbidometric assay (Hitachi 902 autoanalyzer; Roche Diagnostics, Mannheim, Germany) (Varghese, Deepa, Rema, & Mohan, 2001). Microalbuminuria was defined as a urine albumin excretion of 30–299 mg/μg of creatinine (Pradeepa et al., 2010). Nephropathy was defined as macro-albuminuria i.e., a urine albumin excretion of ≥300 μg/mg of creatinine (Pradeepa et al., 2010). The DMDSC laboratory is certified by the College of American Pathologists and the Indian National Accreditation Board for Testing and Calibration of Laboratories.

2.1. Retinopathy

Four-field digital retinal colour photography was taken by a trained photographer using a Carl-Zeiss Digital Fundus Camera. The 4 fields photographed were the macula, optic disc and nasal to the optic disc, and superior–temporal and inferior–temporal quadrants of each eye. The grading of retinopathy was done based on the modified Early Treatment Diabetic Retinopathy Study (ETDRS) grading system (Early Treatment Diabetic Retinopathy Study Research Group, 1991). Each eye was graded separately by an ophthalmologist trained in ETDRS grading, at DMDSC. The minimum criterion for diagnosis of DR was the presence of at least one definite microaneurysm in any field of the retina. Photographs were assessed and assigned a retinopathy level and the final diagnosis for each patient was determined from the level of DR of the worse eye using ETDRS final retinopathy scale (Early Treatment Diabetic Retinopathy Study Research Group, 1991; Rema et al., 2005). Briefly, level 10 represents no retinopathy, levels 20 to 50, non-proliferative diabetic retinopathy (NPDR) [Level 20: mild NPDR; levels 30 to 40: moderate NPDR; level 50: severe NPDR] and levels ≥ 60, proliferative diabetic retinopathy (PDR) (Early Treatment Diabetic Retinopathy Study Research Group, 1991).

Diabetic macular edema (DME) was defined as retinal thickening at or within one disc diameter of the centre of the macula or the presence of definite hard exudates (Early Treatment Diabetic Retinopathy Study Research Group, 1985; Wilkinson et al., 2003). DME could be present in both NPDR and PDR stages, but, once PDR was diagnosed, the final severity scale was graded as PDR (Rema et al., 2005). Sight-threatening diabetic retinopathy (STDR) was defined as PDR or DME (clinically significant macular edema) in either or both eyes (Younis, Broadbent, Vora, & Harding, 2003). Where clinically indicated, optical coherence tomography (OCT) was done and appropriate treatment was offered to the subjects (Otani, Kishi, & Maruyama, 1999).

3. Statistical analysis

All statistical analyses were done using SPSS statistical package version 15.0 (SPSS Inc., Chicago, IL, USA). Continuous data are expressed as mean ± standard deviation while categorical data are presented as proportions. Student's t test was used to compare means of continuous variables between subjects with and without retinopathy in T1DM-Y and T2DM-Y groups. Chi square test was used to compare proportions. To assess independent risk factors for diabetic retinopathy and age adjusted prevalence, we used logistic regression models with DR as the dependent variable and reported odds ratios (OR) with 95% confidence intervals (CIs) and percentages. First, variables were independently tested with the outcomes using bivariable analysis and significant variables (p value <0.05) were entered into a multivariable analysis. For all statistical tests, p value <0.05 was considered significant.

4. Results

Diabetic retinopathy was present in 80 (53.3% [95% CI 45.3–61.3]) people with T1DM-Y and 79 (52.7% [95% CI 44.7–60.7]) people with