Incidence and risk of diabetic retinopathy in Emirati patients with maturity onset diabetes of the young (MODY).

Alshafi Mohammad, Adam Buckley
Research Institute, Imperial College London Diabetes Centre, Abu Dhabi, United Arab Emirates

Background: Diabetic retinopathy (DR) is a potentially sight-threatening complication of diabetes mellitus. The incidence and associated risk factors of DR has been studied in primary forms of diabetes but little is known with regards to Maturity Onset Diabetes of the Young (MODY), particularly in Middle Eastern populations.

Aims: We aimed to study the incidence of DR in Emirati patients with MODY and to identify clinical and biochemical risk factors associated with its occurrence.

Method: Patients with diabetes mellitus underwent digital retinal photography at Imperial College London Diabetes Centre, United Arab Emirates (UAE). Retinal photographs were graded according to the NHS Diabetic Eye Screening Programme for severity of DR and presence or absence of maculopathy. Forty-eight patients highly suspected to have MODY were tested for mutations in all known monogenic diabetes genes using targeted next generation sequencing. Clinical and biochemical parameters were reviewed.

Results: Pathogenic MODY mutations were identified in a total of 30 cases, with *HNF1A*, *GCK*, *HNF4A*, *HNF1B*, and *CEL* in 50%, 26.7%, 16.7%, 3.3% and 3.3%, respectively. Retinal disease of any grade was found in 26.7% (n=8) of individuals with a genetic diagnosis of MODY, with 75% (n=6) of HNF1A-MODY patients having background (n=4), proliferative (n=1), or stable-proliferative DR (n=1), and 25% (n=2) of HNF4A-MODY patients having background (n=1) or stable-proliferative (n=1) retinopathy. Maculopathy occurred in half (50%) of the HNF1A-MODY cases and all (100%) with HNF4A-MODY. Overall, the incidence rate of any degree of DR in patients with MODY was 880 (270-1490) cases per 10,000 person-years. Significant differences were found in univariate analysis in mean duration of diabetes (14.2±5.3 vs 5.4±6.3years, p=0.002), HbA1c (9.5±1.8% vs 7.1±1.3%, p=<0.001), total cholesterol (TC) (5.3±1.7 vs 4.1±1.0mmol/L, p=0.030), and triglycerides (1.8±1.1 vs 1.0±0.6mmol/L, p=0.018) between individuals with any degree of retinopathy and those without retinal disease. Treatment modality was significantly different in cases with and without any retinopathy (p=0.001), with 50% vs 9.1% receiving insulin. No significant difference in age at onset of diabetes (p=0.640), LDL (p=0.225), albumin- creatinine ratio (p=0.208) were observed. Mean age at examination, blood pressure (BP), estimated glomerular filtration rate, and BMI in individuals with or without retinopathy were 32.2±9.9 vs 19.9±10.9years, 114.5±9.8/69.4±7.4 vs 112.9±12.1/67.1±10.5mmHg, 122±31.6 vs 120.3±25mL/min/1.73m2, 24.1±2.4 vs 22.5±5.3kg/m2, respectively. In multivariate Cox regression incorporating TC:HDL ratio, systolic BP and HbA1c, increased TC:HDL was independently associated with significantly increased hazard of any degree of retinopathy (HR 3.96 (1.08 - 14.5)).

Discussion: The incidence rate of any degree of retinopathy in Emirati patients with primarily *HNF1A* and *HNF4A* MODY appears increased in comparison to recently published incidence rates for Type 2 Diabetes (200 to 300 per 10,000 person-years) and comparable with rates reported in Type 1 Diabetes (500 to 660 cases per 10,000 person-years). The high incidence of retinal disease in HNF1A MODY highlights the importance of retinal screening from the time of diagnosis, along with early identification of potential MODY cases in order to optimise blood glucose quickly and effectively.