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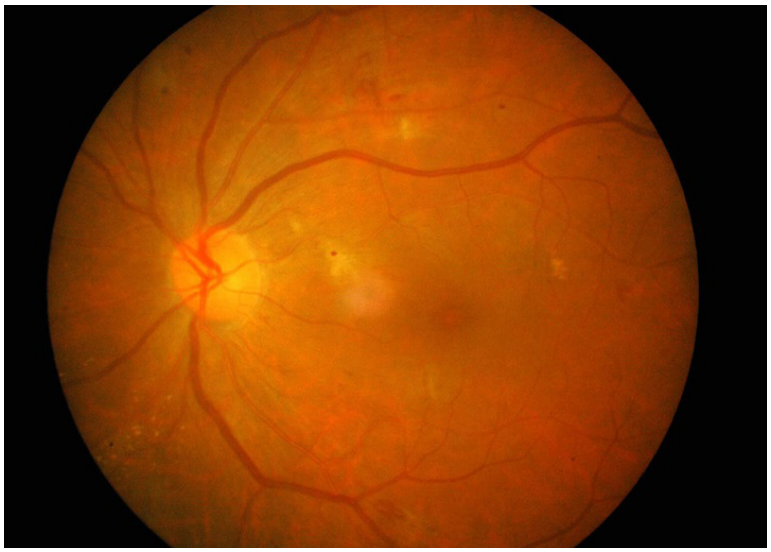
In this issue

Children With Type 2 Diabetes Develop Vision-Threatening Retinopathy Sooner and at a Higher Rate Than Children With Type 1 Diabetes

A retrospective study of a population-based cohort of children (younger than 22 years) diagnosed with diabetes during a 50-year period found that those with type 2 diabetes (T2D) developed vision-threatening retinopathy after a shorter diabetes duration and at a higher rate than did children with type 1 diabetes (T1D).



Retinal image of right eye in uncontrolled type 2 diabetes with decreased visual acuity and hyperglycemia.

"Despite the increasing prevalence of T2D diagnosed in childhood, little is known about the natural history of ocular sequelae in youth-onset T2D compared with T1D," says Brian G. Mohney, M.D., Ophthalmology, at Mayo Clinic in Rochester, Minnesota. "Current pediatric diabetic retinopathy screening follows evidence-based guidelines for children diagnosed with T1D, but data guiding the management of diabetic retinopathy in childhood-onset T2D are limited."

To assess the risk of children developing diabetes-associated ocular complications, Dr. Mohney and fellow researchers used Rochester Epidemiology Project data to conduct a retrospective, population-based medical record review of all residents of Olmsted County, Minnesota, diagnosed with diabetes at ages younger than 22 years between 1970 and 2019. The study appeared in the January 2022 issue of *JAMA Ophthalmology*.

The research team confirmed a diagnosis of T1D for inclusion if the medical record reported a diagnosis of insulin-dependent diabetes mellitus, or T1D, with subsequent treatment consistent with management of T1D. A diagnosis of T2D was confirmed as noninsulin-dependent diabetes mellitus, or T2D. Among 1,362 individuals with a diagnostic code of diabetes before 22 years of age, 606 met inclusion criteria.

Diabetes-associated ocular complications assessed in the study included nonproliferative diabetic retinopathy, proliferative diabetic

Brian G. Mohney, M.D.

retinopathy, diabetic macular edema, a visually significant cataract and the need for pars plana vitrectomy.

COHORT CHARACTERISTICS

During the 50-year period, 606 children were diagnosed with diabetes, yielding an incidence of T1D of 26 per 100,000 children per year and an incidence of T2D of 5 per 100,000 per year. Of the 606 children diagnosed, 525 underwent at least one eye examination and sufficiently met diagnostic criteria to distinguish between T1D (461 participants) and T2D (64 participants).

Cohort characteristics included:

- The mean age at diabetes diagnosis was 12.1 years.
- Of the 525 participants, 261 were female and 264 were male.
- White children (384) constituted a significantly larger percentage of the T1D cohort compared with the T2D cohort (35). There were nine children of Asian descent with T1D and three with T2D and 12 Black children with T1D and 21 with T2D.
- The proportion of female participants in the T2D cohort was significantly higher than that in the T1D cohort.
- Those patients with T2D were more likely to have a blood pressure of greater than 130/80 mm Hg or be using antihypertensive medications at the initial diagnosis of diabetic retinopathy compared with patients with T1D.
- Diabetes-associated ocular complications occurred in 147 of the 461 children with T1D and in 17 of the 64 children with T2D.

The hazard ratios illustrating the risk between T2D and T1D rates of developing complications were:

- 1.88 for any diabetic retinopathy (nonproliferative or proliferative diabetic retinopathy)
- 2.33 for proliferative diabetic retinopathy
- 1.49 for diabetic macular edema
- 2.43 for a visually significant cataract
- 4.06 for requiring pars plana vitrectomy by 15 years after the diagnosis of diabetes

The prevalence of diabetic retinopathy, including both nonproliferative diabetic retinopathy and proliferative diabetic retinopathy, was 32.6% at 15 years after diagnosis among all patients with documentation of eye examinations during a mean follow-up of 13 years, with 18 individuals dying before 40 years of age.

"In this study, children diagnosed with T2D had a higher risk of developing diabetic retinopathy, developing proliferative diabetic retinopathy and requiring pars plana vitrectomy compared with those diagnosed with T1D," notes Dr. Mohney. "The duration between the diagnosis of diabetes and the development of diabetic retinopathy was shorter in the T2D cohort compared with the T1D cohort, and patients with T2D developed vision-threatening retinopathy at a higher rate than those with T1D.

"This data suggests that the natural history of retinopathy development among youth diagnosed with T2D may differ from that in youth diagnosed with T1D — that patients with T2D may be more susceptible to developing retinopathy than those with T1D despite controlling for diabetes disease duration. Children with T2D may require ophthalmoscopic evaluations at least as frequently as or more frequently than children with T1D to prevent serious ocular complications."

FOR MORE INFORMATION

Rochester Epidemiology Project. *https://rochesterproject.org.*

Bai P, et al. Ocular sequelae in a population-based cohort of youth diagnosed with diabetes during a 50-year period.

Reexamining the Relationship Among Metabolic Syndrome, CCT and Ocular Hypertension

Chronic and progressive, glaucomatous optic neuropathy (GON) results in characteristic cupping of the optic nerve and visual field loss. GON accounts for more than 8% of blindness worldwide.

The most significant risk factor for the development of GON is intraocular pressure (IOP). Ocular hypertension (OHTN) — the presence of elevated IOP without evidence of GON — is also a risk factor for development.

"The only reliable treatment for GON is lowering IOP with medications, laser or surgery. Yet even when successful, these treatments may only delay progression, with side effects and repeated dosing leading to compliance issues and high economic burden," says Gavin W. Roddy, M.D., Ph.D., Ophthalmology, at Mayo Clinic in Rochester, Minnesota. "Lifestyle factors, however, may impact the development of glaucoma, so the prevention or reduction of progression risk through lifestyle modification is an attractive low-risk, high-reward intervention."

Dr. Roddy notes: "Defining a person's overall state of health related to lifestyle is challenging. There are many variables, including underlying genetic predisposition, diet and exercise. Metabolic syndrome (MetS) is a definable endpoint, yet knowledge gaps exist in our understanding of the association of MetS with GON and OHTN."

Multiple mechanisms of disease are common between MetS and GON, and some prior studies suggested an association among MetS and OHTN and GON.

However, prior studies left unclear:

- Whether studies performed in other patient populations, including those of East Asian descent, could be readily applied to patients in the United States who are more likely to consume a Western diet, which is a significant risk factor for MetS
- The contribution of central corneal thickness (CCT), which not only can influence the measurement of IOP but also is an independent risk factor for the development of GON

To address those knowledge gaps, Dr. Roddy and fellow researchers conducted a retrospective chart review using the

Gavin W. Roddy, M.D., Ph.D.

Table. Baseline demographic data.

Of the 38,286 patients who met inclusion criteria, 30,204 **(78.9%) qualified as having MetS**.

Study participants were **57.2% female. Patients without MetS were more likely to be female (73.0%; P < 0.01)**.

Patients without MetS were younger: 62.2% were 40 to 59 years old, compared with **29.9%** of patients with MetS in that age group **(P < 0.01)**.

Patients without MetS were more likely to never have used tobacco (89.4% vs. 83.5%, P < 0.01).

Patients with MetS who never used tobacco were most likely to have dyslipidemia **(94.7%)**, hypertriglyceridemia **(93.0%)** and systemic hypertension **(83.0%)**.

Almost half of patients with MetS **(46%) met all five criteria of MetS**.

More patients with MetS identified as white (**90.8%**) compared with patients without MetS **(89.1%, P < 0.01)**.

Rochester Epidemiology Project, a collaboration of health care providers in Olmsted County, Minnesota, that shares patient medical records, with permission, to researchers. Their findings were published in the *Journal of Glaucoma* in 2021.

PATIENT IDENTIFICATION

Patients were identified as having MetS based on diagnosis codes, laboratory values and medication use, or if they met at least three of the following five previously established criteria:

- Body mass index 27 kg/m^2 or higher, substituted for waist circumference
- Triglycerides greater than or equal to 150 mg/dL, or treatment for or diagnosis of hypertriglyceridemia
- HDL-C less than 40 mg/dL in men, HDL-C less than 50 mg/dL in women, or treatment for or diagnosis of dyslipidemia
- Blood pressure greater than or equal to 130 mm Hg systolic or greater than or equal to 85 mm Hg diastolic, or treatment for or diagnosis of hypertension
- Fasting glucose 100 mg/dL or higher, or treatment for or diagnosis of hyperglycemia

Researchers used International Classification of Diseases (ICD-10 and ICD-9) medical billing codes to identify patients with primary open-angle glaucoma, regular or low-tension glaucoma, pigment dispersion glaucoma, and pseudoexfoliation glaucoma. Any of these conditions that resulted in GON were collectively analyzed and referred to as GON. Researchers identified patients with billing codes of OHTN in a similar fashion.

Baseline demographic data included age, sex, race or ethnicity, and smoking history (Table). In patients with GON or OHTN, researchers reviewed the most recent eye exam and, if available for each eye, documented a logarithm of the minimum angle of resolution conversion for the best corrected or pinhole Snellen visual acuity, IOP, cup-to-disk ratio, and CCT.

CCT'S ROLE

Dr. Roddy summarizes the study outcomes: "After adjusting for baseline demographic data, we concluded that GON was not associated with MetS — and an increasing number of MetS components were also not associated with GON. Patients with GON and MetS, however, did have higher IOP and CCT than those patients without MetS.

"Both before and after adjustment for demographic factors, patients with MetS were more likely to have OHTN. Increasing numbers of MetS components were also associated with OHTN. After IOP was adjusted for CCT, there was no significant association between MetS and adjusted IOP in patients with GON and patients with OHTN. Our study supports prior evidence that MetS is associated with OHTN and also suggests that this association may be related to increased CCT.

FOR MORE INFORMATION

Rochester Epidemiology Project. *https://rochesterproject.org*.

Wu KY, et al. Association of metabolic syndrome with glaucoma and ocular hypertension in a Midwest United States population. *Journal of Glaucoma*. In press. https://journals.lww.com/glaucomajournal/Abstract/9000/Association_of_Metabolic_Syndrome_with_Glaucoma.97481.aspx

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Ophthalmology Update

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Cover Image
Human multicolored iris of the eye animation concept
Credit: CG Alex