

III. OCULAR COMPLICATIONS OF DIABETES MELLITUS

A. DIABETIC RETINAL DISEASE

Diabetic retinal disease, primarily manifesting as diabetic retinopathy and/or diabetic macular edema (DME), is the most common microvascular complication of diabetes.¹⁶⁶ Despite the availability of highly effective treatments, diabetic retinopathy remains a leading cause of moderate and severe visual loss among working-aged adults in the United States and other industrialized countries.

Diabetic retinopathy is often asymptomatic early in the disease and visual loss is primarily due to the development of DME, vitreous hemorrhage, or traction retinal detachment.³⁴ Diabetes duration and sustained hyperglycemia are among the primary risk factors for the development of diabetic retinopathy.¹⁶⁷

The progression of diabetic retinopathy occurs in well-defined stages. It may progress from mild nonproliferative diabetic retinopathy (NPDR), characterized by increased vascular permeability, to moderate and severe NPDR, with vascular closure, to proliferative diabetic retinopathy (PDR), with the growth of new vessels on the retina and posterior surface of the vitreous.

The level of retinopathy does not always correlate with visual function and severe diabetic retinopathy can be present initially without significant visual loss. Identifying the severity level of diabetic retinopathy is important for determining the risk of progression and the appropriate care for preservation of vision. Each level of NPDR is associated with a corresponding risk for progression to PDR and subsequent risk of severe visual loss.

Diabetic macular edema may be present at any severity level of nonproliferative or proliferative diabetic retinopathy. DME is caused by the breakdown of the blood-retinal barrier that leads to intraretinal fluid accumulation in the macula, causing photoreceptor disruption, and, if untreated, increased risk of loss of vision.³⁸

Multiple biological pathways have been implicated in the development of diabetic retinopathy. Current studies have pointed to specific biochemical pathways, molecular mechanisms, and hemodynamic alterations in early diabetes mellitus that include the sorbitol pathway,¹⁶⁸ advanced glycation end-products,¹⁶⁹ protein kinase C activation,¹⁷⁰ oxidative stress,¹⁷¹ inflammatory markers,¹⁷² alteration in retinal blood flow,¹⁷³ and growth factors, such as vascular endothelial growth factor (VEGF).¹⁷⁴ These studies demonstrate that changes in retinal biochemistry and physiology occur long before clinically evident disease is observed.

Early neuronal degeneration may also develop in the inner retina in persons with diabetes before the onset of clinical diabetic retinopathy. Changes in retinal thickness and visual function can be observed with optical coherence tomography (OCT), contrast sensitivity, and pattern electroretinogram testing. It has not been determined if these changes are caused directly by damage from chronic hyperglycemia or from the effects of vascular diabetic retinopathy.¹⁷⁵ (Evidence Grade: D)

1. Epidemiology of Diabetic Retinal Disease and Vision Loss

In the United States, an estimated 40.3 percent of adults ≥ 40 years of age with diabetes have diabetic retinopathy and 8.2 percent have vision-threatening retinopathy (proliferative or severe nonproliferative retinopathy and/or macular edema).¹⁷⁶ The worldwide prevalence of diabetic retinopathy in persons with diabetes is estimated to be 34.6 percent, with 10.2 percent having vision-threatening diabetic retinopathy.¹⁶⁷ In addition, approximately 3.8 percent of individuals in the United States ≥ 40 years of age with diabetes have DME.¹⁷⁷ Globally, 6.8 percent of persons 20 to 79 years of age are estimated to have DME.¹⁶⁷

In 2010, 800,000 people worldwide were blind and 3.7 million were visually impaired due to diabetic retinopathy, an increase of 27 percent and 64 percent, respectively, from 1990 to 2010.¹⁷⁸ The number of Americans aged 40 years or older with diabetic retinopathy and vision-threatening diabetic retinopathy is projected to triple by 2050, from 5.5