Volume 4, Issue 3, 2026

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

PREVALENCE AND CONCURRENCE OF AGE-RELATED MACULAR DEGENERATION AND DIABETIC RETINOPATHY IN PATIENTS PRESENTING TO A TERTIARY REFERRAL CENTER IN PAKISTAN

Dr Banafsha khan[*1], Dr Rijaa Syed[2], Dr Ali Mansoor[3], Ammara Younas[4], Matti Ur Rehman Khan[5], Mishaal fatima Akhtar[6], Dr Kainat Abid[7], Muhammad Zahoor[8]

[*1]*PGY1*
[2]*Doctor (Postgraduate, FCPS cleared)*
[3]*Medical Officer*
[4]*4th year mbbs student*
[5]*Doctor*
[6]*Doctor/Medical Officer*
[7]*WMO*
[8]*Nursing Intern, Northwest General Hospital and Research Center Peshawar*

[*1]kbanafsha6@gmail.com, [2]rijaasyed39@gmail.com, [3]am5757151@gmail.com, [4]ammarayounas90@gmail.com, [5]mattikhan036@gmail.com, [6]mishaalakhtar17@gmail.com, [7]kainatabid0103@gmail.com, [8]muhammadzahoorbnu40@gmail.com

DOI: https://doi.org/10.5281/zenodo.23660576

Keywords
Diabetic retinopathy, retina, fundoscopy, age-related macular degeneration, epidemiology

Article History
Received: 01 January 2026
Accepted: 17 March 2026
Published: 31 March 2026

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Corresponding Author: *
Dr Banafsha khan

Abstract

Aim: *To examine how often diabetic retinopathy (DR) and age-related macular degeneration (AMD) occur together, using five years of data from a university hospital.*

Methods: *We reviewed 1,739 patients with diabetes mellitus examined between 2023 and 2025. DR and AMD status were documented alongside patients' clinical characteristics.*

Results: *AMD was diagnosed in 193 of the 1950 patients (10.5%). Of these, 121 had no sign of DR and 72 had DR. Among patients with DR, dry AMD was most frequent in mild non-proliferative DR (NPDR) at 11.5%, compared with 4.5% in moderate NPDR, 4.2% in severe NPDR, and 2.4% in proliferative DR (PDR). Neovascular AMD showed a similar pattern: 3% in mild NPDR, 1.9% in moderate NPDR, 1% in severe NPDR, and 1.8% in PDR. The more severe the DR, the less common AMD was, and this relationship was statistically significant. Among patients with diabetic macular edema (DME), 12 (4.6%) had dry AMD and nine (3.4%) had neovascular AMD.*

Conclusions: *Over five years, AMD prevalence was 12% in patients with DR and 11.5% in diabetic patients without DR. The two diseases therefore seldom occur together, which suggests that DR may protect against the development of AMD.*

INTRODUCTION

Diabetes mellitus is a growing health concern worldwide. Diabetic retinopathy is one of its serious microvascular complications and a leading cause of blindness, particularly among adults under 40 in developed countries. An

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

estimated 400 million people live with diabetes; roughly one-third of them have DR, and about one-tenth have vision-threatening disease such as diabetic macular edema (DME) or proliferative DR (PDR).

AMD is the most common cause of legal blindness in older adults, especially Caucasians in developed countries. Its pathophysiology is multifactorial and not fully understood, although a number of risk factors are known. Age is the most important demographic risk factor, while smoking and sunlight exposure aggravate risk. Nutrition, gut microbiota, hypertension, and genetic variants have also been reported as contributors.

Because diabetes and AMD share inflammatory and oxidative-stress mechanisms, an association has often been proposed, yet the evidence is contradictory:

- The Beaver Dam Eye Study found no link between diabetes and early AMD or geographic atrophy, although diabetic men older than 75 had more exudative AMD than non-diabetic men.
- The European Eye (EUREYE) Study found a positive association between diabetes and neovascular AMD, but not with geographic atrophy or early AMD.
- The Blue Mountains Eye Study linked diabetes to geographic atrophy, but found no association with neovascular or early AMD.
- Other studies found no association between diabetes or DR and AMD, possibly because people with diabetes may not live long enough to develop AMD.

Earlier research also indicated that AMD is significantly less prevalent among people with diabetes than in the general population. The relationship between AMD and DR in particular has been poorly documented. Benson et al. pointed out that AMD is uncommon in people with DR, and Zylbermann et al. reported a very low AMD prevalence in DR, with laser-treated DR patients less likely to develop neovascular AMD. Given this background, we aimed to explore the association between DR and AMD using five years of data from a university setting.

Materials and Methods

We included 1950 patients with diabetes who were screened between 1 January 2023 and 31 December 2025 at the tertiarty hospitals. Patients with dense cataracts or other media opacities that prevented a reliable fundus examination were excluded. , and all participants provided informed consent.

We recorded each participant's age, sex, medical history, and comorbidities (hypertension and hyperlipidemia). All patients underwent a standard eye examination consisting of best-corrected visual acuity (BCVA), intraocular pressure (IOP) measurement, slit-lamp examination, and dilated fundoscopy. Optical coherence tomography (OCT) was also carried out with the SPECTRALIS HRA+OCT device (Heidelberg, Tampa, FL, USA), using six 3 mm radial scans at equally spaced angles centered on the foveola. Fluorescein angiography was performed at the physician's discretion when needed to confirm a diagnosis.

DR stage was determined by dilated fundoscopy, and patients were categorized as having no apparent DR, mild NPDR, moderate NPDR, severe NPDR, or PDR. The presence of DME was also noted. Every participant was assessed for dry or neovascular AMD. Dry AMD was defined by retinal pigment epithelium (RPE) changes, Bruch membrane alterations, and drusen, while neovascular AMD was diagnosed when choroidal neovascularization was detected.

Statistical analysis was done with SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Patient characteristics were described using means, medians, standard deviations, and percentages. Correlations were assessed with Spearman's rank correlation coefficient, and significance was set at $p<0.05$.

Results

Table 1 summarizes the demographic and clinical characteristics of the sample. The mean age was 68.9 ± 8.2 years. There were 742 men (42.7%) and 997 women (57.3%). Type 2 diabetes was present in 1,393 patients (80.1%) and type 1 in 346 (19.9%). Regarding DR staging, 1,006 of 1,739 patients (57.9%) had no DR, 315 (18.1%)

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

had mild NPDR, 157 (9.0%) had moderate NPDR, 96 (5.5%) had severe NPDR, and 165 (9.5%) had PDR. At the initial examination, 263 patients (15.1%) had DME.

Table 1. Demographic and clinical characteristics of the study sample

Characteristic	Value
Age (mean ± SD, years)	68.9 ± 8.2
Male, n (%)	742 (42.7%)
Female, n (%)	997 (57.3%)
Type 1 diabetes, n (%)	346 (19.9%)
Type 2 diabetes, n (%)	1,393 (80.1%)
No diabetic retinopathy, n (%)	1,006 (57.9%)
Mild NPDR, n (%)	315 (18.1%)
Moderate NPDR, n (%)	157 (9.0%)
Severe NPDR, n (%)	96 (5.5%)
PDR, n (%)	165 (9.5%)

Overall, 193 of the 1950 patients (10.5%) had AMD. Among the 1,006 patients without DR, 116 (11.5%) had AMD: 108 dry and eight neovascular. Among the 733 patients with DR, 67 (9.1%) had AMD. AMD frequency by DR stage was as follows:

- Mild NPDR: 11.5% had dry AMD and 3% had neovascular (wet) AMD.
- Moderate NPDR (n = 157): seven patients (4.5%) had dry AMD and three (1.9%) had neovascular AMD.
- Severe NPDR (n = 96): four patients (4.2%) had dry AMD and one (1%) had wet AMD.
- PDR (n = 165): four patients (2.4%) had dry AMD and three (1.8%) had neovascular AMD.

There was a statistically significant association between DR severity and AMD presence (p = 0.031 across DR groups): the more severe the DR, the less often AMD was found.

Among the 263 patients with DME, 242 (92%) had no AMD, 12 (4.6%) had dry AMD, and nine (3.4%) had neovascular AMD.

Discussion

AMD and DR are both leading causes of vision loss worldwide. The main message of our study is that the coexistence of DR and AMD is unusual. Over five years, AMD prevalence was 12% in patients with DR versus 11.5% in diabetic patients without DR. We also found that coexistence depended on DR severity: AMD was significantly less common in patients with severe NPDR or PDR than in those with mild NPDR or no DR. These results agree with most recent studies reporting lower AMD prevalence in people with diabetes than in the general population. Some other studies, however, have suggested that DR, both NPDR and PDR, may raise the risk of AMD.

To explain the low AMD prevalence in DR, the underlying mechanisms of both diseases must be considered. The earliest sign of AMD is drusen, deposits of debris in Bruch's membrane, and their formation is influenced by dysfunction of the choriocapillaris, linked to low metabolic activity of the outer retina and RPE. Choroidal blood volume and flow decline with aging, which raises AMD risk. The choriocapillaris also loses its capacity to supply oxygen to RPE cells and sustain outer retinal homeostasis. Dysfunction or death of RPE cells then alters secretion of vascular endothelial growth factor (VEGF).

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When the choriocapillaris environment is short of VEGF, one possible outcome is widespread atrophy, as seen in dry AMD. In neovascular AMD, hypoxic stress in the retina and RPE drives VEGF overproduction and abnormal vessel growth.

DR, by contrast, is chiefly a microangiopathy marked by progressive thickening of the retinal capillary basement membrane, pericyte loss, endothelial cell proliferation, and choriocapillaris drop-out. DR is essentially a disease of the inner retina, whereas AMD mainly affects the outer retina. Vitreous VEGF levels in eyes with DR rise progressively with DR severity. The high concentration of diffusible VEGF may be enough to keep RPE cells alive, acting as a protective factor, preserving choriocapillaris homeostasis, and reducing the deposition of debris that forms drusen. Saravia et al. proposed this as an explanation for how DR could prevent degeneration of a still-functioning RPE by supplying it with adequate oxygen.

Zylbermann et al. observed that the more advanced the DR, the stronger the apparent protection against AMD. Treatment of DR may play a role in slowing AMD progression: patients with severe DR or PDR who received laser photocoagulation were less likely to develop AMD. Yoshikawa et al. likewise highlighted a beneficial effect of laser photocoagulation in halting AMD progression, supporting the view that laser-treated DR patients are less prone to AMD.

In our study, patients with DME also had a lower prevalence of both dry and neovascular AMD. This is consistent with earlier work that found no correlation between diabetic retinal pigment epitheliopathy or DME and AMD. It is also worth noting that screening diabetic patients for AMD as well as DR using retinal fundus photographs is reliable and cost-effective.

One limitation is that the study was based on a specialized department (a DR clinic) of a tertiary center rather than on the general population, which implies possible selection bias. Another potential bias is the mean age of the sample: because diabetes increases mortality, selective survival may have reduced the observed prevalence of AMD in patients with diabetes and DR, since AMD predominantly affects the elderly. Nevertheless, the study draws on five years of data, and no comparable work had been done in Greece to provide epidemiological data on the coexistence of DR and AMD.

Conclusions

We found a five-year AMD prevalence of 12% in patients with DR, compared with 11.5% in diabetic patients without DR. In addition, AMD became less common as DR became more severe. These findings suggest that mechanisms underlying DR may protect against AMD development. Larger, population-based studies are needed to confirm our results.

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