COMPLICATIONS OF DIABETIC RETINOPATHY

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Abstract: Diabetic retinopathy (DR) is one of the most significant microvascular complications of diabetes mellitus and a leading cause of acquired blindness in the working-age population in developed countries. The aim of this paper is to comprehensively analyse the main complications of diabetic retinopathy, namely diabetic macular edema (DME), vitreous hemorrhage, retinal detachment, and neovascular glaucoma, as well as the modern therapeutic approaches available for their management. The paper is based on a review of relevant scientific literature, clinical guidelines, and epidemiological data from international and regional sources. The global prevalence of diabetic retinopathy is estimated at approximately 34.6% among all persons with diabetes, with proliferative diabetic retinopathy (PDR) affecting around 10.2% and DME present in approximately 8.6%. In North Macedonia, over 100,000 individuals live with diabetes, and at least 30% are estimated to have signs of retinopathy, with approximately 10% at high risk of vision loss. Diabetic macular edema, caused by increased vascular permeability and disruption of the blood-retinal barrier mediated primarily by VEGF, represents the most common cause of visual impairment in DR. Vitreous hemorrhage results from rupture of newly formed, fragile neovascular vessels in proliferative DR and may lead to permanent vision loss if untreated. Tractional retinal detachment arises through fibrovascular membrane formation and contraction at the vitreoretinal interface. Neovascular glaucoma, driven by anterior segment neovascularization from ischemia-induced VEGF overproduction, results in acute intraocular pressure elevation and rapid optic nerve damage. The primary treatment modalities include anti-VEGF intravitreal injections (ranibizumab, aflibercept), laser photocoagulation (focal, grid, and panretinal), and vitrectomy for advanced cases. Anti-VEGF therapy has revolutionized DME management and is now the first-line treatment, achieving visual acuity improvement of 15 or more ETDRS letters in 34-50% of treated patients. Panretinal photocoagulation remains a cornerstone for PDR, reducing the risk of severe vision loss by 50-60%. Early vitrectomy is superior in type 1 diabetes patients with severe vitreous hemorrhage. The findings underscore that timely diagnosis, regular ophthalmological screening, optimal glycaemic control, and multidisciplinary collaboration are essential for preventing progression and preserving visual function. An estimated 90% of severe vision loss cases related to DR are preventable with appropriate intervention.
Keywords: diabetic retinopathy, macular edema, vitreous hemorrhage, retinal detachment, anti-VEGF. Field:

1. INTRODUCTION

Diabetes mellitus affects over 537 million adults globally and is projected to reach 783 million by 2045 (IDF, 2021). Among its most significant microvascular complications, diabetic retinopathy (DR) stands out due to its direct impact on vision and quality of life. DR is the leading cause of acquired blindness in working-age adults in developed countries, yet it is largely preventable with early detection and appropriate treatment. The purpose of this paper is to review the mechanisms, clinical features, and modern management of the major complications of diabetic retinopathy: diabetic macular edema, vitreous hemorrhage, tractional retinal detachment, and neovascular glaucoma.

2. MATERIALS AND METHODS

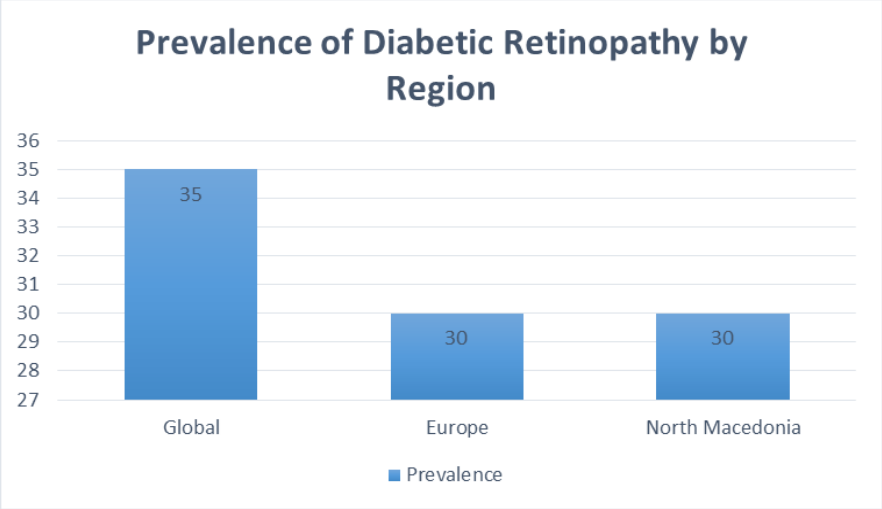
This paper is a narrative review based on analysis of peer-reviewed scientific literature, clinical practice guidelines from the American Academy of Ophthalmology and the American Diabetes Association, as well as epidemiological data from the World Health Organization, the International Diabetes Federation, and the Institute of Public Health of North Macedonia. Literature was searched across PubMed, Google Scholar, and institutional databases using the terms: diabetic retinopathy, macular edema, vitreous hemorrhage, retinal detachment, neovascular glaucoma, anti-VEGF, laser photocoagulation, vitrectomy. Articles published in the past 15 years were prioritized, with inclusion of landmark studies regardless of publication date.

3. RESULTS

EPIDEMIOLOGY

Approximately 30-40% of all persons with diabetes have some form of DR (Yau et al., 2012). Globally, 93 million individuals live with DR, of whom 28 million have proliferative disease (WHO, 2020). In Europe, between 25% and 35% of diabetic patients have DR, with notable disparities between Western and Eastern European countries (Einarson et al., 2018). In North Macedonia, at least 30,000 of an estimated 100,000 people with diabetes show signs of retinopathy, with approximately 2,000 new cases registered annually, of which at least 400 are in a proliferative phase (Institute of Public Health, 2021).

Graphic 1: Prevalence of Diabetic Retinopathy by region



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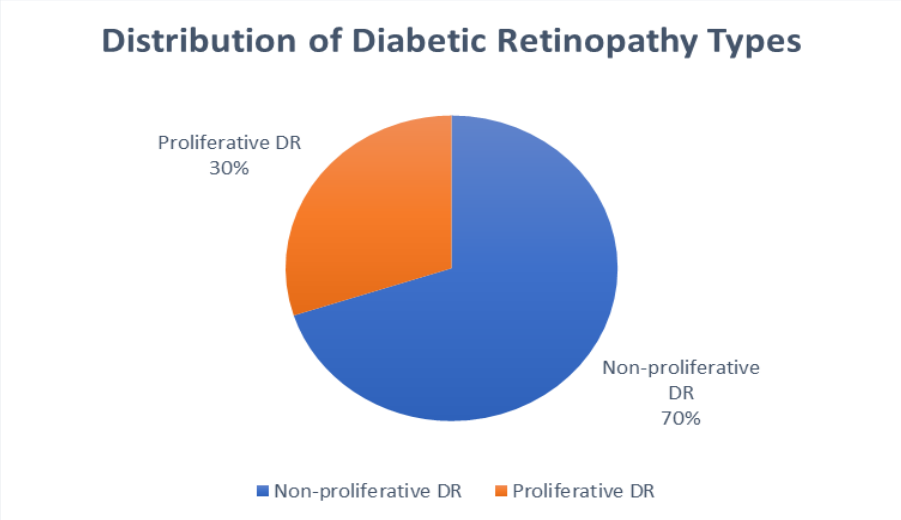
Graphic 2: Distribution of Diabetic Retinopathy types



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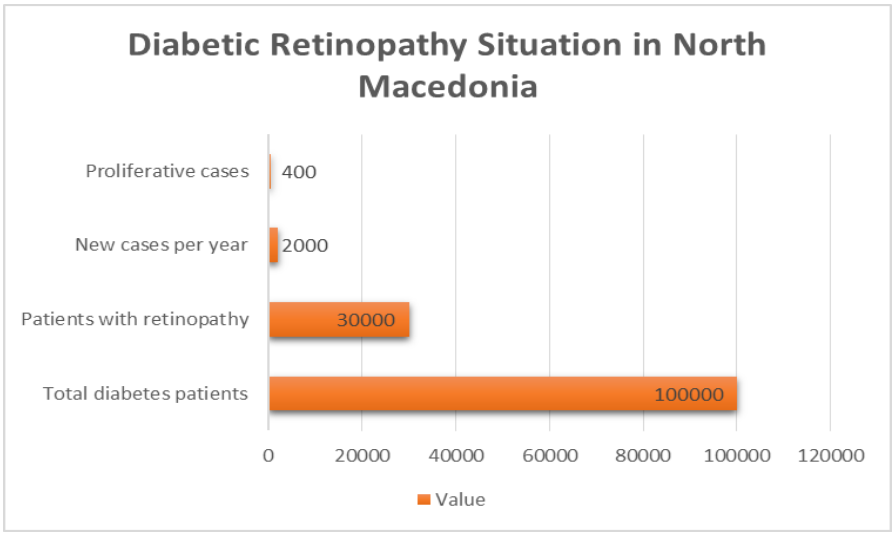
Graphic 3: Diabetic Retinopathy situation in Nort Macedonia



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DIABETIC MACULAR EDEMA (DME)

DME results from disruption of the inner and outer blood-retinal barriers, predominantly mediated by VEGF-induced hyperpermeability. Fluid accumulates in the intraretinal and/or subretinal space of the macula, which is responsible for central vision and color discrimination. DME is clinically significant (CSME) when retinal thickening is present within 500 μm of the foveal center, or when hard exudates with adjacent thickening are detected. Symptoms include blurred central vision, metamorphopsia, and reduced reading ability. Optical coherence tomography (OCT) is the gold standard for diagnosis, providing cross-sectional imaging with micrometer resolution. Fluorescein angiography delineates zones of leakage and capillary non-perfusion.

VITREOUS HEMORRHAGE

Vitreous hemorrhage (VH) results from rupture of neovascular vessels in proliferative DR. These newly formed vessels lack pericytes, have absent tight junctions, and grow into the vitreous cavity. Mechanical triggers such as physical exertion, blood pressure fluctuation, or Valsalva maneuver can cause their rupture. Clinically, patients experience sudden, painless vision loss, floaters, or complete visual blackout. Small hemorrhages may resorb spontaneously within weeks to months. Massive or non-resolving hemorrhage can lead to fibrovascular membrane formation, tractional retinal detachment, and neovascular glaucoma. B-scan ultrasonography is essential when fundus examination is precluded by the hemorrhage.

TRACTIONAL RETINAL DETACHMENT (TRD)

TRD is the dominant form of retinal detachment in DR. Retinal ischemia drives VEGF upregulation and neovascularization at the vitreoretinal interface. Fibrovascular membranes form alongside new vessels and, upon contraction, exert traction on the retina, separating the neurosensory retina from the retinal pigment epithelium. Subretinal fluid accumulates in the created space. Clinically, patients report photopsia, floaters, and a progressive curtain over the visual field. Macular involvement results in central vision loss. TRD in DR is typically chronic and progressive. OCT detects subretinal fluid and subtle traction, while B-scan ultrasound is indispensable when VH obscures the fundus view.

NEOVASCULAR GLAUCOMA (NVG)

NVG is a severe secondary glaucoma arising from extensive retinal ischemia. VEGF diffuses anteriorly, stimulating rubeosis iridis (neovascularization of the iris) and angle neovascularization. Fibrovascular membranes obstruct trabecular meshwork outflow and may form anterior peripheral synechiae, leading to acute intraocular pressure elevation, often exceeding 50-60 mmHg (normal: 10-21 mmHg). Patients experience intense ocular pain, headache, corneal edema, conjunctival injection, nausea, and rapid optic nerve damage. Even with aggressive treatment, many patients sustain significant permanent vision loss, making prevention through timely panretinal photocoagulation critical.

TREATMENT

Anti-VEGF therapy (ranibizumab, aflibercept) is the current first-line treatment for center-involving DME. Clinical trials (VIVID, VISTA, RIDE, RISE) demonstrated that anti-VEGF achieves ≥15-letter BCVA improvement in 34-

50% of patients compared to laser monotherapy. Anti-VEGF also induces regression of neovascularization in PDR, though the effect is temporary and often combined with panretinal photocoagulation (PRP). PRP, applying 1,200-1,600 laser spots to the peripheral retina, reduces severe vision loss risk by 50-60% by decreasing metabolic demand and VEGF production from peripheral photoreceptors (Diabetes Control and Complications Trial Research Group, 1993; UKPDS Group, 1998). Vitrectomy is indicated for non-resolving vitreous hemorrhage (3-6 months), tractional retinal detachment, and DME refractory to anti-VEGF. Modern 23G/25G/27G minimally invasive techniques allow sutureless surgery with faster recovery. The DRVS study showed that early vitrectomy is superior in type 1 diabetes patients with severe vitreous hemorrhage.

4. DISCUSSION

The last two decades have witnessed a paradigm shift in DR management. The introduction of anti-VEGF therapy transformed DME treatment, while improved understanding of VEGF biology has provided mechanistic insight into all major complications. The regional disparities in DR prevalence and outcomes, particularly the higher burden in Eastern Europe and Balkan countries, reflect differences in healthcare infrastructure, screening programme implementation, and access to anti-VEGF therapy. In North Macedonia, the absence of a national screening programme and limited OCT availability—concentrated mainly in Skopje—result in delayed diagnosis, often at the proliferative stage. Implementing mobile screening units, telemedicine platforms, and AI-assisted fundus image analysis could substantially improve early detection in rural areas. The finding that 90% of severe DR-related vision loss is preventable underscores the need to shift resources towards primary prevention: optimal glycaemic control (HbA1c <7%), blood pressure management, lipid control, and regular annual ophthalmological examinations for all diabetic patients.

5. CONCLUSIONS

Diabetic retinopathy and its complications represent a major, yet largely preventable, public health burden. Diabetic macular edema, vitreous hemorrhage, tractional retinal detachment, and neovascular glaucoma share a common pathogenetic mechanism centred on VEGF-driven microvascular dysfunction. Modern therapies—anti- VEGF injections, laser photocoagulation, and vitrectomy—are highly effective when applied in a timely manner. Early and regular ophthalmological screening, combined with optimal metabolic control and a multidisciplinary approach integrating endocrinology, ophthalmology, and patient education, is essential for preventing progression and preserving visual function. Patients with type 1 diabetes should undergo ophthalmological examination within 5 years of diagnosis and annually thereafter; patients with type 2 diabetes should be examined immediately upon diagnosis and annually. Investment in national screening infrastructure, digital registries, and healthcare professional training is urgently needed, particularly in countries with transitional health systems such as North Macedonia.

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