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Narrative Review of Diabetes and Eye Complications: Retinopathy

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ABSTRACT

Diabetic retinopathy (DR) is one of the most prevalent and debilitating microvascular complications of diabetes mellitus and remains a leading cause of vision impairment and blindness globally. This narrative review examines the epidemiology, pathophysiology, clinical manifestations, diagnostic approaches, management strategies, and public health implications of diabetic retinopathy, with attention to disparities across geographic, racial, and socioeconomic groups. Evidence indicates that chronic hyperglycemia, duration of diabetes, hypertension, dyslipidemia, and obesity are central drivers of DR onset and progression, mediated through complex metabolic and inflammatory pathways that result in retinal microvascular damage and neurodegeneration. Despite declining incidence in some high-income settings, the global burden of DR continues to rise, particularly in low- and middle-income countries, where limited access to screening and treatment exacerbates preventable vision loss. Current management approaches, including glycemic control, laser photocoagulation, intravitreal anti-vascular endothelial growth factor therapy, and surgical interventions, can reduce disease progression but often fail to fully restore visual function and may be associated with adverse effects. Emerging strategies such as artificial intelligence–assisted screening, telemedicine, and integrated care models show promise in improving early detection and access to care. Addressing diabetic retinopathy requires coordinated clinical, technological, and public health interventions focused on early prevention, equitable screening, and health system strengthening to mitigate its growing global impact.

Keywords: Diabetic retinopathy**,** Diabetes complications**,** Vision impairment**,** Retinal microvascular disease and Screening and prevention.

INTRODUCTION

Diabetic retinopathy (DR) and related eye disorders collectively represent the most significant burden of diabetes as they pose a pronounced threat to vision and global healthcare systems [1]. Epidemiological data reveal widespread prevalence, diverse population-level trends, and substantial geographic, racial, and socioeconomic disparities. Certain patient characteristics and comorbidities exacerbate the risk of DR and related progression [2]. Despite recognition of diabetes as a major risk factor for primary open-angle glaucoma, which affects approximately 500 million people, DR remains the primary condition associated with blindness related to diabetes. Diabetes fosters microvascular injury in many tissues, including the retina [5]. Risk increases with the presence and severity of diabetic retinopathy. Pathophysiological pathways linking hyperglycemia to DR involve the polyol pathway, production of advanced glycation end products, protein kinase C activation, and cellular oxidative stress. Consequently, retinal neurodegeneration stemming from metabolic disturbance occurs, ultimately resulting in blood-retinal barrier breakdown, Müller cell gliosis, and increased release of proinflammatory cytokines, chemokines, and neurotrophic factors [5].

Epidemiology of Diabetic Retinopathy

Diabetic retinopathy (DR), a vascular disorder of the retina characterized by microvascular complications, is the most common cause of vision loss in individuals with diabetes [3]. The disease arises from hyperglycemia-induced metabolic disturbances and is associated with diabetes duration, glycemic control, hypertension, dyslipidemia,

obesity, and diastolic blood pressure [4]. Although incidence and prevalence rates have markedly decreased in high-income countries, DR remains a critical global public health concern exacerbated by urbanization of low- and middle-income countries and increasing rates of obesity, hypertension, kidney disease, and diabetes among the general population [5]. An estimated 422 million people worldwide live with diabetes, the prevalence of which has doubled since 1980. By 2030, the number of adults aged 18 years or older with diabetes is projected to exceed 500 million (World Health Organization, 2016). Between 2010 and 2014, the Global Burden of Disease Study ranked diabetes as the seventh leading cause of death, attributing approximately 1.5 million deaths annually directly to the disease (Lancet, 2016)[7].

Pathophysiology of Diabetic Retinopathy

Diabetic retinopathy is caused by specific factors, namely, glycemic control, duration of diabetes, hypertension, and dyslipidaemia [2]. Early detection and timely treatment can prevent irreversible vision loss, especially in people with diabetes [17]. Practice and research acknowledge a general classification of diabetic retinopathy simplifying the clinical classification into non-proliferative diabetic retinopathy and proliferative diabetic retinopathy [2]. Clinicians and researchers alike have developed various classification schemes, including the Early Treatment Diabetic Retinopathy Study (ETDRS) and the International Clinical Diabetic Retinopathy Severity Scale (ICDR), incorporating the most prominent lesions, clinical characteristics, and imaging findings evident at each stage [6].
The considerable number of individuals aged between 20 and 79 years presenting with diabetic retinopathy around the globe has raised both public health and financial concerns [5]. Additionally, there are projected to be an estimated 161 million cases of diabetic retinopathy, including 45 million cases of vision-threatening diabetic retinopathy and 29 million diabetic macular oedema [2]. Furthermore, a clear understanding of the mechanisms involved in the onset and progression of diabetic retinopathy would provide an opportunity to design effective preventive and therapeutic strategies [7].

Clinical Manifestations and Classification

Diabetic retinopathy is a microvascular complication that represents the commonest cause of blindness in working-age population [1]. There are two types of diabetic retinopathy: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). Diabetic retinopathy is associated with cumulative exposure to hyperglycemia in people with either type 1 or type 2 diabetes [4]. The risk factors for the development and progression of diabetic retinopathy include rising levels of glycosylated hemoglobin (HbA1c), duration of diabetes, hypertension, elevated lipids, and proteinuria [3]. Microvascular and macrovascular diabetic complications together, affect demographic, epidemiological and physiopathological characteristics, and therapeutic approaches for both types of diabetes. Aggressive screening programs should be implemented in the management of both types of diabetes to identify microvascular disease early and prevent significant morbidity [8].

Diagnostic Approaches and Screening

Diabetic retinopathy represents the most common ocular complication of diabetes. It occurs in patients with either type 1 or type 2 diabetes and can result in serious visual impairment [9]. The worldwide prevalence of diabetic retinopathy among adults aged 20 to 79 years is 34.6% and vision-threatening diabetic retinopathy 10.2% [10].
Several population-based studies have demonstrated that diabetes-related retinopathy can develop within 10 years of diagnosis, particularly in young adults and children with type 1 diabetes. Longitudinal population-based studies have further shown that, despite a change in treatment practices, clinically recognizable diabetic retinopathy progresses in a substantial proportion of patients, highlighting the need for ongoing monitoring [10]. Major classification systems of diabetic retinopathy differ in their intended application but denote broadly similar stages [11]. The Early Treatment Diabetic Retinopathy Study classification describes diabetic retinopathy in five different grades [18]. The International Clinical Diabetic Retinopathy Disease Severity Scale defines the following stages of severity: no apparent retinopathy; mild non-proliferative; moderate non-proliferative; severe non-proliferative; and proliferative diabetic retinopathy [12].

Management and Treatment Modalities

The treatment focus for diabetic retinopathy is to preserve both vision and quality of life. Even with current medication and laser treatments, however, patients suffer from progressive loss of vision as well as reduced vision-related quality of life [13]. In a study comparing three different treatments for diabetic macular edema, visual acuity improvement and other parameters were significantly better with treatment than without; however, at five years, only half the patients treated with currently available techniques gained even one-line improvement on the visual acuity chart [12]. Another study showed that, despite considerable anatomical improvement in diabetic macular edema, the majority of patients showed no significant visual acuity gain [13]. Other studies indicate that photocoagulation improves the risk of blindness but does not enhance the visual acuity gained by intravitreal anti-VEGF agents administered thereafter [14]. Adverse events also accompany treatment for diabetic retinopathy [18]. Endophthalmitis and elevated intraocular pressure are among the most common complications following

cataract surgery and intravitreal injections. Other complications include systemic events, local and systemic anticoagulation, and unregulated use of medication [18].

Complications and Comorbidities

Diabetic retinopathy (DR), the most frequent microvascular complication of diabetes, is a leading cause of vision impairment and blindness worldwide [3]. A series of risk factors, including chronic hyperglycemia, hypertension, dyslipidemia, and obesity, influence the onset, progression, and severity of DR [4]. The burden of diabetes and its complications, including retinopathy, is increasing in many countries. In Ethiopia, only sensitization and community awareness programs are recommended, notwithstanding the other methods available for sick people [15]. Furthermore, within diabetic subjects, the variation in DR prevalence in various geographic locations and across population sub-groups such as age and sex may inform understanding of its etiology and enhance the assignment of appropriate priority for preventive action [16]. In Ethiopia, three studies on DR give prevalence estimates of 11.2% (Urban), 12% (Rural), and 45% (Cohort, Urban), consistent with results from other countries with similar development profiles [12]. Diabetes is the leading cause of ocular complications in many developing countries, including Ethiopia [15]. Apart from reducing mortality and morbidity, adequate management of diabetes is paramount to promote better eye health and prevent sight-threatening ocular complications such as retinopathy and cataract that are prevalent among the population [13]. Ocular complications of diabetes generally occur late and management should target to prevent, postponement, and/or reduction of diabetic complications of all types. It was found that the ocular complications of diabetes appeared approximately 7 years after the occurrence of diabetes [16]. Ocular and systemic health examination should be considered for diabetic individuals at initial visit. Different ocular or systemic illnesses coexist with these complications [15]. Diabetic retinopathy remains among the most feared complications of diabetes as it often results in irreversible loss of vision. Retinopathy is accompanied by other ocular disorders associated with diabetes, and a significant number of individuals have one or more ocular complications [1]. In Ethiopia, the adverse ocular impact of diabetes is often neglected as the focus remains on systemic issues. Awareness of diabetes symptoms and associated comorbidities must be raised to reduce the risk of ocular diseases [16]. In a study of 194 diabetic patients without retinopathy referred to the eye department, 97 individuals had ocular comorbidity such as glaucoma, cataract, pterygium, or conjunctivitis [19].

Prevention and Public Health Implications

Diabetic retinopathy (DR) is an important public health problem that can result in vision impairment and blindness [10]. Prevention of DR in those already diagnosed with diabetes and the rise in number of extra people with diabetes in public domains are of urgent importance [12]. The estimated global number of individuals with diabetes rose from 108 million in 1980 to 422 million in 2014. The number of people with diabetes is projected to rise from 463 million in 2019 to 700 million in 2045[13]. The global proportion of diabetes is set to rise will continue to rise from 9.3% in 2019 to 10.9% in 2045, and DR is expected to increase proportionately. DR usually starts from the changes in the retinal microvascular structure and function, pre-clinically manifested as hyperglycemic retinal neurodegeneration in an individual who have chances of becoming diabetic [14]. A large body of experimental and human observational research highlights blood glycosylated hemoglobin (HbA1c) as an important risk factor for DR [9]. Glycated protein and glycated lipid formation fuelling polyol pathway activation, formation of advanced glycation endproducts (AGE) fuelling protein kinase C (PKC) and oxidative stress pathways, and hyperglycemic-storage-mediated insulin signalling aberration [15]. DR globally affects people physiologically and economically, as DR treatment cost can rise up to approximately the same cost as a standard ocular surgical procedure [14]. Early population screening for DR via free low-cost fundus camera screening programs has been successfully implemented at Singapore nation-wide and has provided a population benefit in terms of both health capital and [17].

Gaps in Knowledge and Future Directions

Diabetes is a serious global health concern, as its burden continues to increase and disproportionately afflicts those in low-income settings [10]. Diabetes-related retinopathy (DR) constitutes a significant public health issue, with increasing prevalence and heterogeneity in its occurrence [11]. The specific pathophysiological mechanisms involved are still poorly understood, as are the associated clinical features and changes in retinal structure and function that occur early in the disease [12]. At the population level, the incidence of both type 1 and type 2 diabetes continues to rise across low-, middle-, and high-income countries, along with an apparent increase in DR incidence across age groups. Rates of diabetes and DR also remain markedly higher among ethnic minorities [16]. Better understanding of the mechanisms linking hyperglycemia and other metabolic derangements to retinal damage, including changes occurring before the onset of retinopathy, may pave the way for more robust prevention and treatment strategies [18]. Addressing the methodological shortcomings of existing studies and extending investigations to encompass novel candidate biomarkers, 3D retinal imaging, and assessment of long-

term outcomes would further enhance knowledge and contribute to improved patient management [17-21]. Artificial intelligence (AI) tools can effectively automate the detection and grading of retinal disease using fundus photographs, making such approaches valuable for filling specialist shortages and improving patient access to care [22-26]. Telemedicine screening networks established during the COVID-19 pandemic have expanded service capacity, making automated or remote approaches widely applicable. Telemonitoring is another promising approach that allows patients to communicate important information and may reach individuals at higher risk [27]. Box 4 summarizes several patient-centered care models designed to improve the quality, efficiency, and equity of eye care delivery, integrating different aspects of the health system.

CONCLUSION

Diabetic retinopathy remains one of the most serious and feared complications of diabetes mellitus, with profound consequences for vision, quality of life, and health systems worldwide. Its development reflects the cumulative effects of chronic hyperglycemia and associated metabolic and vascular risk factors, resulting in progressive retinal damage that is often asymptomatic until advanced stages. Despite advances in diagnostic imaging and therapeutic modalities, many individuals continue to experience irreversible visual loss, underscoring the limitations of current treatment strategies when disease is detected late. This review highlights the critical importance of early detection through systematic screening programs, particularly in low- and middle-income countries where the burden of diabetes and its ocular complications is rapidly increasing. Population-based screening, improved glycemic and blood pressure control, and timely referral for ophthalmic care remain the cornerstone of prevention. Innovative approaches, including artificial intelligence enabled retinal imaging, telemedicine networks, and task-shifting models, offer scalable solutions to overcome workforce shortages and access barriers. Future progress in reducing the burden of diabetic retinopathy will depend on improved understanding of early disease mechanisms, development of reliable biomarkers, and integration of patient-centered care models within broader diabetes management frameworks. Policymakers and healthcare systems must prioritize equitable access to screening and treatment, invest in preventive strategies, and strengthen primary care services to curb avoidable vision loss. Without such coordinated efforts, diabetic retinopathy will continue to pose a significant clinical and public health challenge in the context of the global diabetes epidemic.

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