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The worldwide epidemic of diabetic retinopathy

Yingfeng Zheng[1,2], Mingguang He[1], Nathan Congdon[1]

Diabetic retinopathy (DR), a major microvascular complication of diabetes, has a significant impact on the world's health systems. Globally, the number of people with DR will grow from 126.6 million in 2010 to 191.0 million by 2030, and we estimate that the number with vision-threatening diabetic retinopathy (VTDR) will increase from 37.3 million to 56.3 million, if prompt action is not taken. Despite growing evidence documenting the effectiveness of routine DR screening and early treatment, DR frequently leads to poor visual functioning and represents the leading cause of blindness in working-age populations. DR has been neglected in health-care research and planning in many low-income countries, where access to trained eye-care professionals and tertiary eye-care services may be inadequate. Demand for, as well as, supply of services may be a problem. Rates of compliance with diabetes medications and annual eye examinations may be low, the reasons for which are multifactorial. Innovative and comprehensive approaches are needed to reduce the risk of vision loss by prompt diagnosis and early treatment of VTDR.

Key words: Compliance, diabetic retinopathy, services

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The prevalence of Diabetic Retinopathy (DR) is intimately linked to the upsurge in prevalence of diabetes.[1-5] Diabetes was once thought of as a disease of the affluent but it has now reached epidemic proportion in both developed and developing countries. Currently, at least 366 million people worldwide have diabetes, and this number is likely to increase as a result of an aging global population, urbanization, a rising prevalence of obesity, and sedentary lifestyles.[1] While recent improvement in diabetes treatment has decreased macrovascular mortality, more patients with diabetes live long enough for DR and vision-threatening diabetic retinopathy (VTDR) to develop.[6]

What is the Prevalence of Diabetic Retinopathy?

A recent systematic review of 35 population-based studies showed that the prevalence of DR, proliferative diabetic retinopathy (PDR), diabetic macular edema (DME), and VTDR among individuals with diabetes is 34.6%, 7.0%, 6.8%, and 10.2%, respectively.[7] By extrapolating these results to the global number of diabetics, we can estimate that the number of people with DR will grow from 126.6 million in 2011 to 191.0 million by 2030, and the number of people with VTDR will increase from 37.3 million to 56.3 million, if no urgent action is taken.

In the American National Health and Nutrition Examination Survey (NHNES, 2005–2008), 28.5% of diabetic patients had some degree of DR, 4.4% had VTDR.[8] Similar prevalence estimates are seen in many other developed countries.[7] In the not-so-distant past, DR was thought to be relatively uncommon in developing countries like China and India.[9,10] It has now become apparent that many low- and middle-income countries are also confronting this challenge, and the prevalence is similar or even higher than that reported in developed countries.[7] China is a good example of a country facing both, the epidemic of diabetes and DR. China is estimated to have 92.4 million adults with diabetes, and a recent report in rural China showed that 43% of the patients with diabetes already have retinopathy and 6.3% have VTDR.[6,11]

What is the Incidence of Diabetic Retinopathy?

While accurate figures are difficult to obtain for the incidence of DR, the results of the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) showed that the overall incidence of DR in a 10-year interval from 1980–1982 to 1990–1992 was 74%, and among those with DR at baseline, 64% had more severe retinopathy and 17% developed PDR.[12] These figures were 89%, 76%, and 30%, respectively among the younger-onset group (diagnosed before age 30 years); and 67%, 53%, and 10%, respectively, among the older-onset group who did not use insulin. In the 25-year follow-up of the WESDR type-1 diabetes group, almost all patients (97%) developed DR, and among these, 42% progressed to PDR, 29% developed macular edema (ME) and 17% had clinically significant ME.[13,14]

Has there been a Decline in the Prevalence/ Incidence of Diabetic Retinopathy among those with Diabetes?

In the past three decades, the prevalence and incidence of DR among patients with type 1 diabetes have declined in the US, Australia, and other developed countries. A systemic review of 28 studies showed that participants reported on between1986 and 2008 had a lower incidence of PDR (2.6% vs. 19.5%) and severe visual loss (3.2% vs. 9.7%) at 4 years, compared with the 1975–1985 cohort, although the results do not differentiate type-

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1 from type-2 diabetes.[15] This decline may be due to improved glycemic control in recent decades, but it is too early to know if the decrease is on-going. There is also a lack of data to compare the effects of different treatment regimens (e.g., multiple daily injections versus continuous subcutaneous insulin infusion) on the incidence and progression of DR. In the WESDR cohort, the annual incidence of PDR declined from 3.4% to 1.4% among the type-1 diabetes, and the incidence of clinically significant macular edema (CSME) from 1.0% to 0.4%.[12] Nevertheless, this decline may not occur in low- or middle-income countries where the programs on early HbA1c screening and effective blood sugar and blood pressure control are unavailable. While studies have documented a decline in the incidence of DR among those with type-1 diabetes, the trend of DR among patients with type-2 diabetes remains uncertain.

What are the Risk Factors Associated with Diabetic Retinopathy?

Cross-sectional and longitudinal studies have identified some factors associated with a higher risk of DR. These include hyperglycemia, hypertension, dyslipidemia, duration of diabetes, pregnancy, puberty, and cataract surgery.[16] Despite the importance of glycemic control in diminishing the progression of DR, intensive glycemic control appeared to increase mortality among participants in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial,[17] which raises concerns over the care of persons with type-2 diabetes who are at high risk of cardiovascular events, and highlights the need for close collaboration between diabetologists and ophthalmologists.

Is there a Socioeconomic Gradient in Prevalence of Diabetic Retinopathy?

The impact of socioeconomic inequality on health is now well recognized, and people with diabetes are unlikely to be immune. However, the extent to which socioeconomic status may influence patients with DR is unclear. In fact, the relationship between socioeconomic status and DR is only apparent in some but not all studies.[10,18,19] This observed weak or absent social gradient may be attributed to a number of competing influences, including lifestyle, health behaviors, attitude, mortality rate, and health-care systems. In many low- and middle-income countries, for example, higher socioeconomic groups are more likely to consume western foods and pursue a sedentary lifestyle than their poorer counterparts; these factors may counter the beneficial effects of good diabetes care and glycemic control among the rich.[19] These findings do not negate the importance of developing and evaluating ways of addressing the underlying sociocultural factors that render individuals vulnerable to DR and DR-related visual impairment.

What are the Consequences of Diabetic Retinopathy?

DR is rapidly emerging as a global health issue that may threaten patients' visual acuity and visual functioning. Although treatment of established retinopathy can reduce the risk for visual loss by 60%,[20] DR remains the leading cause of blindness among working-age adults in the world. The proportion of blindness attributable to DR ranges from 3–7% in much of South-East Asia and the Western Pacific region to 15–17% in the developed regions of the Americas and Europe.[21] In addition to the direct consequences of visual impairment, DR, particularly in its vision-threatening stages, has a substantial and negative impact on patients' emotional well-being, although the exact mechanisms remain to be determined.[22]

The financial costs of DR are mounting. Depending on the prevalence of diabetes and the organization of particular health systems, diabetes is estimated to account for 11.6% of the annual health-care budgets in most countries, and DR makes a big contribution to this figure.[23] In the United States alone, the direct annual costs of DR were estimated to be USD$490 million in 2004.[24] In Sweden, the annual average healthcare cost of any DR, PDR, and DME amounts to USD$93.6, USD$334.1, and USD$280.8, respectively, per patient.[25] Health economic data on the cost of DR in low- and middle-income countries is currently not available.

Challenges and Opportunities

Capacity

Globally, the backlog of diabetes has far outstripped the capacity and resources to implement DR eye care. Although many low- and middle-income countries (e.g., India and China) have begun to tackle the leading causes of remedial blindness, that is, cataract, the need for DR eye care remains largely unaddressed.[3,4] The fundamental problem is lack of access to high-quality ophthalmologists, health care resources and facilities. Many countries still have one ophthalmologist per million population (1% of the scale in the United States), with the vast majority of ophthalmologists residing in large cities, leaving many rural and remote areas underserved. Even if basic eye screening is available, many patients with DR still have no adequate access to laser treatment. For example, a 2003 national survey in China showed that 90% of public hospitals have no lasers facilities.[26]

There is no simple solution to build capacity. In addition to poverty eradication programs, new health care delivery strategies should be promoted to meet the demand for DR eye care. Telemedicine, the use of telecommunication and information technologies to provide clinical health care at a distance, represents the single most promising technology in the context of rural DR care. It provides a tool whereby scattered delivery systems may be transformed into a comprehensive DR network that can capitalize on many of the resources, tools, and training already in place in urban areas. In regions where tertiary eye care services (e.g., laser and vitrectomy surgery) are not available, special referral mechanisms and education programs should be established so that advanced cases of DR can receive adequate treatment. There is also a need for the development of a low-cost, portable, and easy-to-operate laser devices.[27]

Sustainability

Sustainability is traditionally defined as the ability to maintain the benefits of eye care programs and support such programs financially, even when both technical and financial assistance are no longer provided from the outside. To be sustainable, a service or program should become politically and culturally

integrated into the local environment. While "Sustainability" has, to an extent, become a buzzword in research and program proposals, provisions for this vary widely between eye care programs in developing areas. In the majority of developing countries, DR eye care does not exist in isolation from other eye care (cataract, refractive error, etc.) and opportunistic screening remains the predominant model. The operation of DR care depends on the sustainable development of the entire eye care program. Meanwhile, some countries (e.g., UK and Singapore) have begun to implement stand-alone DR eye care programs to tackle the burden of the disease, resulting in the issue of sustainability becoming even more important.

Management capacity is critically important for a sustainable DR eye care program, but this has been neglected in health-care planning and research. Many previous research projects have focused simply on technical aspects of DR eye care and service delivery (e.g., screening settings, grading thresholds, photographic methods, referral intervals), but without a sufficient appreciation of the role of good management. A local DR screening clinic should not only adapt to a country's resources and available health-care infrastructure, but it should also operate like a business in a competitive marketplace to optimize services and maximize returns. Like chronic disease management, management of DR requires a high level of organization over a patient's lifetime. Project managers and investigators should be encouraged to identify differences between DR eye care centers, and undertake investigations to evaluate market-driven strategies and business models, so that programs can operate without grant funding or charitable contributions. Moreover, health economic data should be made available to evaluate the cost-effectiveness of different business models under various scenarios. Logistics cost is one of the key areas for cost saving, and a well-organized program should constantly review and improve its supply chain operations (e.g., how to identify DR patients, notify results, offer education and treatment, and then repeat annual fundus examination or laser treatment). Although sustainability is critically important, continuous charitable care may still be needed in rural areas and refugee camps with insufficient financial or human resources to provide eye care.

Key performance indicators

Many epidemiologic studies have used a self-reported history of "yearly eye examination after pupillary dilation" as a measure of access to DR eye care.[3,4] This measure, however, may not be an ideal health metric to reflect either the quality or the quantity of DR eye care. In fact, the "Key Performance Indicators (KPIs)" of DR eye care have been variably defined. At the point of care, the performance of a DR program is influenced by technology, resources, and patient-related factors and at the structural level, by health systems and policy regulations. Due to the complex interplay of these factors, the KPIs of DR eye care are often poorly characterized. In assessing DR screening, the KPIs should go beyond diagnostic indexes such as sensitivity and specificity. Important factors such as uptake; personal training; quality assurance; and follow up of the cases with DR (e.g., time from referral to ophthalmic consultation, time from listing to laser treatment, time from screening event to ophthalmic consultation and the proportion of referred patients who fail to be present for ophthalmic review), should be continuously evaluated. The UK National Screening Committee has recently produced a catalogue of KPIs for DR eye screening programs in England,[28] a move that may stimulate similar proposals elsewhere. In addition to screening, other key questions involved in the evaluation of DR eye care are as follows: What is patients' accessibility to DR eye screening? What are the quality, training and practice standard of health providers? How successful are the strategies used to improve compliance and self-management? Are the programs financially and logistically sustainable?

Another concern is that many policy makers and NGO funders ignore the equity implication of population-based eye care delivery. Patients' health beliefs and attitudes are known to have an important influence on participation in screening and follow up, and these effects vary significantly between socioeconomic classes and ethnic groups. Therefore, efforts must be made to ensure that any regional or national DR eye care program does not exacerbate health inequalities.

Physician-patient relationship

Lack of adherence to diabetes vision care guidelines among patients with diabetes has been recognized as a persistent and complex health issue. In the US, one-third of the patients with diabetes failed to follow vision care guidelines (absence of a dilated eye examination),[29]and in developing countries like China, nonadherence has reached crisis proportion—more than 60%.[3] Nonadherence affects patients of all ages and it can lead to avoidable visual impairment. There are numerous socioeconomic, behavioral, medical, and policy-related factors that contribute to this problem; among these, low health literacy level in patients is a significant contributing factor to noncompliance with treatment, which ultimately leads to worse glycemic control and higher rates of retinopathy. There is therefore, a need to develop materials and tools to facilitate diabetes education and management in patients with low literacy. Additionally, adequate patient outreach and reminder programs may be useful to improve compliance. Injecting an incentive mechanism into eye care programs may be helpful in improving compliance to annual eye examination and laser treatment as well, though the effectiveness and sustainability of such interventions has rarely been evaluated. Lessons from behavioral economics suggest that an incentive program is more attractive if it provides immediate rather than delayed rewards, while success is less likely in the face of immediate as opposed to delayed costs.[30]

The physician–patient relationship is a two-way street, and both parties are accountable to each other. The challenge of improving physician's compliance with guideline-recommended care is not new. In a recent survey in urban Indonesia, less than 50% of the patients with diabetes reported being told of the need for eye examinations by their physicians.[4] Nonadherence to guidelines may occur due to physicians' lack of awareness of the rationale behind the guidelines, lack of time for communication, lack of reimbursement, lack of resources, and a combination of these factors. Furthermore, many residency projects and continued medical education (CME) programs offer limited education about effective communication. Finally, without organizational support, reimbursement mechanisms and computerized tracking systems, effective physician–patient communication may be very difficult.

The Way Forward

The natural history and global burden of DR are well-known. Prevention of diabetes is the best approach for the prevention of DR, but it will require fundamental social and political changes. Among those with diabetes, good glycemic and blood pressure control, regular ophthalmic examinations, and timely laser treatment for macular edema and proliferative retinopathy can markedly reduce the risk of visual impairment. Public health initiatives will be required to make affordable DR screening available and initiatives in education will be needed to improve patient compliance with ophthalmic examinations and facilitate follow ups. Efforts are needed to strengthen the capacity of existing national and local institutions to provide screening services, to train eye-care personnel, and to develop low-cost interventions to improve compliance. Investment is urgently needed to build sustainable business models and evaluate their cost-effectiveness. Current management of DR eye care networks lacks a scientific basis and measurable KPIs; electronic medical records (EMR) may represent an effective approach to monitor performance and accountability. The challenge will be to implement new, practical and sustainable strategies to curb the rising tide of DR.

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