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Projection of Diabetic Patients Retinopathy in Hidalgo State-México, through 2030

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Abstract

Purpose: To estimate the progression of diabetic retinopathy (DR) using a dynamic mathematical model after a comprehensive dilated eye exam at a primary care facility.

Procedures: A dynamic model was built for the projection of DR cases in patients with type 2 diabetes mellitus in primary health care facilities in Hidalgo, Mexico. Data were collected in 2010. A blood sample was taken after an overnight fast to determine glucose levels and ophthalmologists performed a comprehensive dilated eye exam with a portable ophthalmoscope (direct and indirect ophthalmoscopy). We used a dynamic model to estimate patients with DM. The model includes demographic effects (population growth and migration), and considers intervals of one year, starting in 2010 and ending in 2030. A difference equation system was used.

Main Findings: The prevalence of DR in 2010 was 33.3% (29.9% NPDR and 3.4% PDR). For 2030, if these conditions remain the same, an increase of 116.3% is expected. This means a general prevalence of 72.1% in this population.

Conclusions: An alarming increment of DR was estimated for 2030. To avoid this complication in people living with diabetes, preventive policies are needed and the care of diabetic patients in primary health facilities must be strengthened. This will yield a lower cost since patients will not require surgery.

Keywords: *Diabetic Retinopathy; Estimation; Primary Health Care; Health Services; Mexico*

Introduction

Diabetes and hypertension are the leading causes of death in adults. In 2012, they represented 82% of premature deaths and 68% of total deaths, of which three-fourths occurred in low- and middle-income countries [1]. In 2016, among member countries of the Organization for Economic Co-operation and Development (OECD) [2], Mexico ranked first in diabetes prevalence (15.9%), and in 2012, according to the National Survey of Health and Nutrition (ENSANUT) 2012, the prevalence of diabetes was estimated at 9.17% (9.67% in women, 8.60% in men) [3]. These figures show an alarming increase in diabetes.

One of the most important aspects of chronic illness is to achieve adequate control of the disease to avoid complications that impair quality of life, and consequently, the country's socioeconomic development. This has been seen in developed countries, where half of the

patients with chronic disease have adequate metabolic control [4]. In Mexico, only one in five patients with diabetes achieve this [5,6]; therefore, there is a likelihood of complications including diabetic retinopathy (DR), and an increase in costs for health systems.

It has been estimated that the annual cost for care of obesity, diabetes, and cardiovascular disease fluctuates between 78,000 and 101 billion pesos. Indirect costs associated with loss of productivity are between 73,000 and 101 billion (Gutiérrez-Delgado, Guajardo-Barrón and Río, 2012), and out-of-pocket expenses 72.951 billion, which possibly involve catastrophic expenses and impoverishment due to health issues [7].

Unfortunately, DR is the most common microvascular complication of diabetes mellitus (DM) and it represents the most frequent cause of blindness in individuals between 20 and 74 years of age [8,9]. DR starts developing at least 7 years before the diagnosis of type 2 diabetes (DM2) [10]. Studies in Mexico report a prevalence of DR between 21.3% and 33.3% [11,12].

The most important risk factors for developing DR are constantly high glucose levels, a decreasing hematocrit, an increase in serum lipids, time of evolution of DM, high albuminuria levels and pregnancy [9,13,14]. DR progresses from non-proliferative diabetic retinopathy (NPDR), which can be mild, to moderate or severe NPDR, and proliferative diabetic retinopathy (PDR), which is characterized by growth of new blood vessels in the retina and the posterior surface of the vitreous [9,10].

DR not only has social repercussions, such as a decrease in the quality of life of patients but also financial repercussions [15]. In the United States, blindness due to DR, and its related costs, were calculated at $ 500 million USD annually [16]. With regard to this situation, projection analysis of the prevalence and incidence of DR allows determining the disease burden, which can be helpful for the health system. However, the prevalence and possible continuing increase in obesity will continue to cause an increase in DM and DR making it necessary for decision makers and policy planners to estimate future health costs and needs [17,18].

In Mexico, the standard for diabetes care (NOM-015) considers actions to prevent vision loss as a result of DR and recommends a fundus examination at the time of diagnosis and annually afterwards. Individuals who have retinopathy should be referred to secondary care [19].

In Health Services Hidalgo, there are DM care clinics that provide comprehensive care and comprehensive dilated eye exams. However, in clinical practice, eye exams are not carried out in all units, and when patients perceive a decrease in visual acuity they visit secondary care units, private services or do not receive treatment. Against this background, the need to identify future scenarios that allow the healthcare decision maker to propose strategies to prevent and adequately treat patients with this complication arises. Therefore, the objective of this study is to estimate, using a dynamic mathematical model, DR progression from comprehensive dilated eye exams in primary care facilities.

Methods

The present study was performed in Hidalgo State, Mexico and was approved by the Ethics and Research Committees of the Health Services. In 2010, five sanitary jurisdictions were chosen and a random subsample of 117 patients with DM2 was estimated from clinical records. We considered a random sample with a margin of error equal to 0.1 and a confidence coefficient equal to 0.95 (n = 96); therefore, our sample size satisfies these assumptions and is statistically representative of the population of diabetic patients in Hidalgo State.

The selected patients were sent to the health center of each jurisdiction and were informed about the study, its procedures and benefits. The ones who decided to participate were scheduled and provided written inform consent; later, ophthalmologists performed a comprehensive dilated eye exam under mydrias is using topic medication with tropicamide and phenylephrine with a portable ophthalmoscope (direct and indirect ophtalmoscopy). At the end of the examination, 2% pilocarpine was applied to reverse the mydriatic effect. Qualified personnel performed all the procedures. To determine the presence and severity of DR, the classification proposed by the Global

Diabetic Retinopathy Project Group was used [20]. Patients with a diagnosis of DR, depending on severity, were given indications according to their clinical status (evaluation at one year or 6 months).Some cases were referred to the General Hospital of Pachuca for specific treatment.

A dynamic model was built to estimate patients with DM. The model included demographic effects (population growth and migration), and considered intervals of one year, starting at 2010 and ending in 2030. A difference equation system, similar to Boyle, Thompson, Gregg, Barker, and Williamson [21] was used [22].

A compartmental model was used, assuming that the diabetic population without retinopathy is one compartment, the diabetic population with non-proliferative retinopathy is another compartment, and the diabetic population with proliferative retinopathy is a third compartment. These compartments are mutually exclusive. Since the assessment is done in fixed periods of time (years), a discrete-time model is proposed. Thus, it is assumed that if there is a transition from one compartment to another over a period of time, it would be recorded in the following assessment.

If X (t-1) represents the number of patients with diabetes without retinopathy at time t-1, then the number of patients with diabetes without retinopathy at time t, will be the number of patients with diabetes who had already been counted at time t-1, plus the number of newly registered patients with diabetes: $X(t) = \alpha_1 X(t-1)$.

If Y (t-1) represents the number of diabetic patients with non-proliferative retinopathy at time t-1, then the number of diabetic patients with non-proliferative retinopathy next year would be those at time t-1 ($\alpha 2Y(t-1)$) plus a fraction of patients with diabetes who did not have retinopathy ($\beta X(t-1)$): $Y(t) = \alpha_2 Y(t-1) + \beta X(t-1)$.

If Z (t-1) represents patients with diabetes with proliferative DR at time t-1, then the number of patients with proliferative DR one year later, will be formed by those who did not have DR, by those with NPDR, and a fraction who already had PDR: $Z(t) = \alpha_3 Z(t-1) + \gamma Y(t-1) + \eta X(t-1)$.

This model has the disadvantage of using constant transition rates, which work well for short periods of time (eg, 5 years). Another disadvantage is that we do not have sufficient data to calculate the transition rates of our population; therefore, we used data from another similar population [23].

The values of the model are annual and the transitions occur in the time interval (t-1, t]. When considering an autonomous difference equations system, we are assuming that the coefficients of the transition matrix are all constant.

X(t): represents the number of diabetic patients without retinopathy at time t.
Y(t): represents the number of diabetic patients with non-proliferative retinopathy at time t.
Z(t): represents the number of diabetic patients with proliferative retinopathy at time t.

We considered a transition matrix, similar to that described in Boyle., *et al*. [21] and S. Wild, Roglic, Green, Sicree, and King [18], given by

$$\begin{array}{c} \\ X(t-1) \\ Y(t-1) \\ Z(t-1) \end{array} \begin{array}{c} \begin{array}{ccc} X(t) & Y(t) & Z(t) \end{array} \\ \begin{pmatrix} \alpha_1 & 0 & 0 \\ \beta & \alpha_2 & 0 \\ \eta & \gamma & \alpha_3 \end{pmatrix} \end{array}$$

Where:

α_1: Increased rate of people with DM.

α_2: Increased rate of people with non-proliferative retinopathy.

α_3: Increased rate of people with proliferative retinopathy.

β: Increased rate to non-proliferative retinopathy.

η: Increased rate to proliferative retinopathy.

γ: Increased rate from non-proliferative to proliferative retinopathy

Notice that the linear difference autonomous system of first order includes the demographic effect; thus the system is:

$X(t)= \alpha_1 X(t-1) + f_X(t-1)$

$Y(t)= \alpha_2 Y(t-1)+\beta X(t-1) + f_Y(t-1)$

$Z(t)= \alpha_3 Z(t-1)+\gamma Y(t-1)+\eta X(t-1) + f_Z(t-1)$

This system is in the form $\mathbf{X}(n) = \mathbf{A}\mathbf{X}(n-1)$ where:

$$\boldsymbol{X}(n) = \begin{pmatrix} X_1(n) \\ \vdots \\ X_k(n) \end{pmatrix}$$

and $\boldsymbol{A} = \begin{pmatrix} a_{11} & \cdots & a_{1k} \\ \vdots & \vdots & \vdots \\ a_{k1} & \cdots & a_{kk} \end{pmatrix}$

with $\mathbf{X}(n) \in \mathbf{R}^k$, $\mathbf{A}$ a real non-singular matrix, f_X, f_Y, f_Z represents demographic effects in each group.

The system is considered autonomous (time invariant) if the coefficients from matrix A are constant. In this case, the system can be solved by using the Discrete Putzer Algorithm. With the information gathered, the initial conditions were: X (0) = 82,000, Y (0) = 35,000, and Z (0) = 4,000.

Assuming these rates are constant, to create the projection, the difference equation system was solved using MatLab (R209B) with the following parameters:

α_1=1.07, α_2=1, α_3=1, β=0.12, η=0.054945, and γ=0.05714. f_X, f_Y, f_Z were calculated with an algorithm proposed by Larios-Ferrer (2012).

Results

The prevalence of DR in 2010 was 33.3% (Figure 1), which represents 29.9% of NPDR (71.4% were minor cases), and 3.4% of PDR. In 2030, if the conditions are the same, a general prevalence of 72.4% will be seen. We expect 796,740 patients with DR, more than those recorded in 2010.

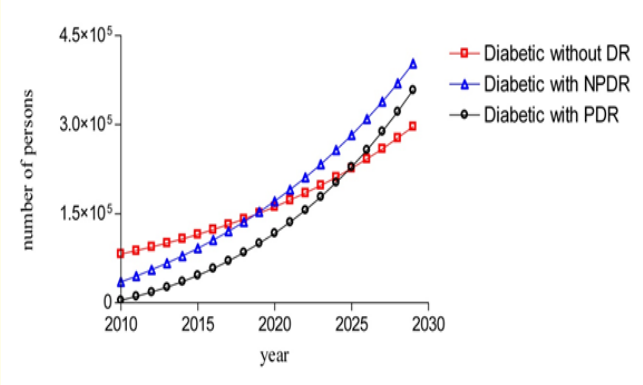

Figure 1: *Estimated progression of patients with diabetic retinopathy for 2010 to 2030.*

With this model, if we modify some values in the set of parameters, the model will show the effect of an intervention on the rate of progression to DR. Therefore, with the intervention, the new parameters values are $\beta = 0.0876$, $\eta = 0.04010985$, and $\gamma = 0.0417122$. Figure 2 shows the dynamics of the system with the intervention. In 2020, patients with NPDR will decrease 21.5%, and patients with PDR, 31.3% (in comparison with no intervention). In addition, in 2030, the patient with NPDR will decrease 24.7% and the patient with PDR, 35%.

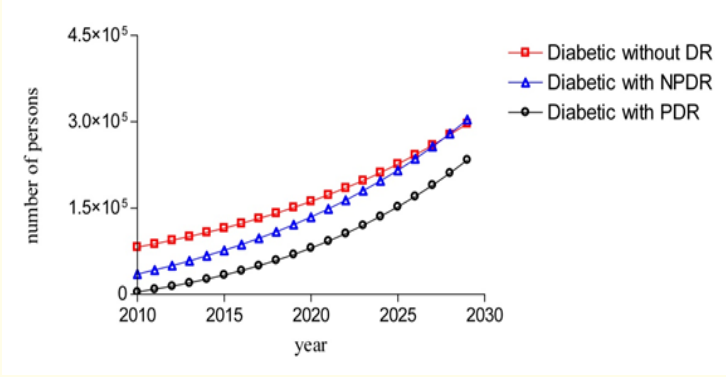

Figure 1: *Estimated increase of patients with diabetic retinopathy with an intervention from 2010 to 2030.*

Discussion

Our findings are in accordance with other results [11]. Furthermore, we assumed that progression rates were affected in the same way and remain constant during intervention. By using these new values, in 2020 we will observe a reduction of 21.5 % in the number of patients with NPDR, which means 36,708 patients less than those without an intervention. We observed a reduction of 31.24% in patients with PDR (36,527 patients less than those without intervention). In 2030, if the progression rate remains the same, we will observe a 24.8% reduction in patients with NPDR, which means 108,918 patients less than those without intervention, while 35% less patients with PDR were observed; this represents 139,443 patients less than those without intervention.

Our results suggest that this kind of intervention, only metabolic control, is an efficient method for modifying progression rates of any type of DR in the short term, but it is insufficient in the long term. The mathematical model describes the behavior of population with DM and some complications associated to DM [24]. Our results are consistent with that of other studies [21,25,26]. Thus, a high number of complications associated with DM appear during the first years after detection of the disease. Future increases in the number of persons with diabetes will likely lead to significant increases in the number of individuals with DR [27].

Previous models for diabetes forecasts have linearly extrapolated historical prevalence trends. Others have built dynamic models incorporating incidence, mortality, and migration. A discrete, three-state Markov model stratified by age, sex, and race/ethnicity projected an approximate doubling of prevalence in the United States by 2050 [8]. In 2006, Boutayeb., *et al*. [25] presented a mathematical study of the size of a population of diabetes mellitus patients and the number of patients with complications. This is a continuous model composed of a differential equations system.

We believe that the modeling methods described here could be used to estimate future DR prevalence as well as the impact of interventions to reduce the disease. The model could be used to analyze other diseases and compare other regions. The main goal of the Health Services will be to reduce the number of patients who develop DR and its progression by developing more efficient intervention policies. There is scientific evidence that shows that annual eye evaluations are costly and add little benefit compared with other plausible alternatives [28].

Prevention programs aimed at improving proliferative retinopathy and macular edema in diabetic individuals will not only result in substantial savings but also in cost-effective prevention of blindness [9]. Biennial ophthalmologic screening for DR is more cost-effective than other routine health interventions [28,29].

The Mexican federal government has established services that prevent, detect and care for chronic non-communicable diseases (CNTD) in Mexico [30] including guidelines that establish a comprehensive dilated eye exam annually in patients with DM [19]. However, in Mexico, treatment for DR was not included in the Universal Catalog of Health Services (CAUSES, in Spanish) of the Social Protection in Health System (SPSS, in Spanish), even though it represents an acceptable cost-effectiveness [31,32].

The limitations of this study were that individual clinical variables associated with the development of DR such as glycemic and blood pressure control, time of evolution of DM, and family history, among others, were not considered. In addition, demographic effects were not considered in the dynamics of the system. Even so, the impact of progression without control measurements was observed.

Our projections may help policy makers anticipate future demands for health care resources and possibly guide the development of targeted interventions. Medical treatments, surgeries, the necessary equipment, and human resources will be more expensive than the investment that prevention represents.

Conclusions

The future increase in the number of people with diabetes will probably mean a significant increase in DR, glaucoma, and cataracts. The implementation of policies that prevent DR will allow a lower investment cost due to the care of patients who do not require surgery.

Our results can help decision makers prevent the future demand of health care resources and guide the development of specific interventions such as the establishment of a program for prevention of DR and the training of primary care physicians in comprehensive dilated eye examination.

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Conflicts of Interest

None declared.

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Volume 5 Issue 2 February 2017