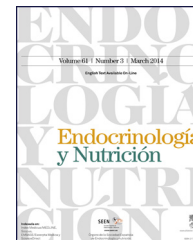




ENDOCRINOLOGÍA Y NUTRICIÓN

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EDITORIAL

The epidemiology of type 1 diabetes: Helping to fit the puzzle pieces[☆]



Epidemiología en la diabetes tipo 1: ayudando a encajar las piezas del puzle

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Epidemiology studies both the different factors involved in disease occurrence, frequency, mode of distribution, and course, and the necessary means to eradicate or prevent such factors. In type 1 diabetes mellitus (T1DM), epidemiology provides essential data about prevalence, incidence, and morbidity and mortality to help us improve patient care, which is the ultimate goal of any medical activity.

The prevalence of T1DM worldwide ranges from 0.8 to 4.6/1000 population, and is 1–1.5/1000 in most cases. As regards its incidence, differences have been reported by country, race, diagnosis or birth season, age, and sex.

In 2013, the International Diabetes Federation published the sixth edition of its Atlas,¹ which includes data from 219 countries. The incidence of T1DM in children ≤14 years of age ranges from 0.1/100,000 population/year in Papua New Guinea and Venezuela to 57.6/100,000 population in Finland. The results provided show a 576-fold variation between the populations analyzed worldwide. By race, non-Hispanic white subjects are the racial group with the greatest incidence of T1DM, followed by blacks, Hispanic whites, and Asians. The greatest incidence of T1DM is found in colder months, while the season with the greatest birth incidence is spring.²

Incidence also varies according to age group and sex. It is greater in childhood as compared to adulthood. The

highest incidence is found in the group aged 10–14 years, and values subsequently decrease until the last decades of life.³ In people older than 15 years, a greater incidence is seen in males, while the results in younger people are different in countries with a high or low incidence of T1DM.⁴

On the other hand, according to data reported by the EURODIAB group,⁵ its incidence in Europe has increased in recent decades, with a mean annual increase of approximately 3.5%. In Navarre, its incidence increased fourfold between 1975 and 2012.⁶ In North European countries, this increase has halted in recent years.⁷

The above described variations may reflect a different degree of genetic susceptibility to diabetes, or be due to a different exposure to environmental risks factors. It is known that T1DM is associated with genes of the major histocompatibility complex HLA, class II, DR4 and DR3, and that the greatest genetic susceptibility corresponds to the combination of both the DR3 and DR4 alleles. However, several studies have shown that most cases occur in children with low-risk HLA genotypes. In an attempt to identify the triggering environmental factors, the influence of socioeconomic level (the higher the level, the greater the incidence), association with viruses (especially enteroviruses), various components of diet (cow milk albumin, vitamin D, breast-feeding, wheat gluten, vitamin E),⁷ the composition of intestinal microbioma, and maternal factors during pregnancy have all been analyzed. These analyses have provided no conclusive results regarding the etiopathogenesis of T1DM, nor have allowed for its prevention.²

The morbidity of T1DM is caused by its acute and chronic complications. Public information and education campaigns, as well as diabetes education for already diagnosed patients,

[☆] Please cite this article as: Forga L. Epidemiología en la diabetes tipo 1: ayudando a encajar las piezas del puzle. Endocrinol Nutr. 2015;62:149–151.

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are important in preventing acute complications. The chronic complications can only be managed if the factors influencing their occurrence and progression are known.

Microangiopathy is characteristic of T1DM. It has recently been shown that both retinopathy (DR) and nephropathy (DN) have two etiopathogenic mechanisms. DR has both a microvascular and a neurological component, with retinal involvement.⁸ DN has a predominantly vascular mechanism, which reflects systemic atherosclerosis—resulting in a decreased glomerular filtration rate without albuminuria—and another classical mechanism, glomerulosclerosis, with albuminuria and no impairment in glomerular filtration rate until the advanced stages.⁹ The prevalence of DR in T1DM is approximately 50% at 10 years and 70% at 20 years from disease onset. The prevalence of DN 20 years from disease onset ranges from 20% to 40%. Diabetic neuropathy represents a heterogeneous group of changes causing various clinical manifestations, although its most common presentations are sensorimotor peripheral polyneuropathy and autonomic neuropathy. The form of diagnosis is essential to adequately assess the prevalence rates given in the different studies (20–50% for both sensorimotor peripheral polyneuropathy and autonomic neuropathy).

In diabetic triopathy (DR, DN, and diabetic neuropathy) it has been reported, with some differences between pathologies and authors, that factors related to its occurrence and progression include: blood glucose control, age at diagnosis, diabetes duration, high blood pressure, smoking, dyslipidemia, and genetic makeup.¹⁰ Among the modifiable factors, since the DCCT/EDIC study we know that improved blood glucose control decreases the occurrence and progression of microangiopathy. The term “metabolic memory” has been coined for the persistence of this effect over time.¹¹ As a control objective, it is recommended that blood glucose levels be maintained as closely to normal as possible, with an HbA1c value <7% in most consensuses. Moreover, if HbA1c is maintained at <7.6%, proliferative DR and persistent macroalbuminuria may possibly be prevented for 20 years.¹²

Although macroangiopathy is not a characteristic of diabetes, macrovascular complications in T1DM occur early, are more diffuse, and have a faster course and greater mortality, especially in patients younger than 40 years. Patients with T1DM have at least a 10-fold greater increase in cardiovascular diseases as compared to age-matched non-diabetic patients. In addition, no differences are seen in cardiovascular risk between men and women with T1DM. The factors associated with microangiopathy include nephropathy, high blood pressure, smoking, dyslipidemia, disease duration, poor blood glucose control, inadequate diet, sedentary lifestyle, obesity, and insulin resistance.¹⁰

People with T1DM have an increased mortality risk (relative risk: 3.82; 95% confidence interval [CI]: 3.41–4.29). At 20 years of age, men and women with T1DM have a lower life expectancy of 12.9 (95% CI: 11.7–14.1) and 11.1 years (95% CI: 10.1–12.1) respectively compared with that of young people of the same age with no DM. Reports as to whether mortality from cancer is increased or not in patients with T1DM provide conflicting results. Before 50 years of age, acute complications are the most common cause of death. From the age of 50 onwards, chronic diseases predominate, particularly cardiovascular disease.¹³ Blood glucose control

and nephropathy significantly contribute to this outcome. However, in the absence of kidney disease and with a theoretically adequate control (HbA1c <7), all-cause mortality continues to be more than two times greater as compared to the general population (hazard ratio [HR]: 2.36; 95% CI: 1.97–2.83), and cardiovascular mortality is almost three times greater (HR: 2.92; 95% CI: 2.07–4.13). And when HbA1c is $\geq 9.7\%$, the HRs are: 8.51; 95% CI: 7.24–10.1 and 10.46; 95% CI: 7.62–14.37 respectively.¹⁴ Thus, although mortality rates of T1DM have been decreasing in recent decades, particularly in patients younger than 15 years and compared to the period prior to 1990, they are still high and, in addition to blood glucose control, high blood pressure and dyslipidemia, there are other factors involved that warrant the need for epidemiological research.

On the other hand, knowledge of the incidence and prevalence rates of T1DM and its complications facilitates the planning and management of the human and financial resources available in those fields where they are most needed. It also makes it possible to assess the efficacy of preventive campaigns. Therefore, such data are indispensable for healthcare management and planning. In the first few years after the diagnosis of T1DM, resources are used for outpatient care, drugs, and self-monitoring. There are no chronic complications. Only acute complications, financially non-expensive unless they require hospital admission, may occur. Despite the preventive information campaigns carried out, a significant proportion of patients with T1DM still have ketoacidosis at diagnosis. In Navarre, these represent one fourth of patients (25.3%). Costs subsequently double due to inpatient treatment of chronic complications. Mean cost per patient with T1DM in the first year after diagnosis is approximately 3000 euros. During follow-up, if no chronic complications occur, the cost is approximately 1.300 euros/person/year. In patients with chronic complications, hospital admissions, and social expenses, the mean cost may increase to 3.300 euros/patient/year.¹⁵

Some countries have national registers that allow for deeper epidemiological research into T1DM. Such registers are available in five Spanish autonomous communities (of which only Catalonia and Navarre include patients above pediatric age), but there is no national register for Spain as a whole. The Epidemiology Group of the Spanish Diabetes Society is now working to try and compile such a register. A Spanish register could not only provide the data that enabled us to answer important questions, but this information would in turn generate more questions requiring more answers. We would be making an attempt to fit the pieces together, as if we were doing a giant jigsaw puzzle.

Funding

Studies on the epidemiology of type 1 diabetes mellitus in Navarre discussed in this editorial were funded by two grants to research projects, an initial grant from the Department of Health of the Navarre government (53/2008) and a subsequent grant from Instituto de Salud Carlos III (PI10/02715).

Conflicts of interest

The author states that he has no conflicts of interest.

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