

Clinical and social impact of the diabetes mellitus epidemic

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SIGNIFICANCE OF DIABETES MELLITUS

The incidence and prevalence of diabetes mellitus (DM) is increasing in recent years. Wild et al.¹ estimated in 2004 the overall number of diabetic patients in the world, calculating that by 2025 up to 366 million people may have DM, particularly type 2 DM. Interestingly, India, China, Indonesia, Pakistan, or Bangladesh are among the countries where DM is experiencing a greater increase, together with «developed» countries such as the US, Italy, and Japan.

The impact of DM on population health stems from its high prevalence, implying high social and financial costs resulting from the occurrence over time of many microvascular and macrovascular complications with progression of the natural history of the disease. This will result in a high comorbidity that will lead to very high mortality rates in the population affected.

DM IN SPAIN

In Spain, recent studies have estimated the prevalence of type 1 DM (DM-1) at approximately 0.3% of the total population, but the prevalence of type 2 DM (DM-2) DM2 is much higher, approximately two million people.

DM distribution by autonomous communities is not uniform, ranging according to adjusted data from 2.8% in La Rioja and 3.4% in Asturias up to 7.3% in Andalusia and 8.1% in the Canary Islands.²

Some studies have estimated the overall prevalence of DM in the Spanish population at approximately 7%. The estimated figure depends on the criteria used to diagnose DM. Rodríguez-Panós et al.³ reported in 2000 a 9.8% prevalence of DM in the Spanish population using blood glucose levels of 126 mg/dL or higher as a criterion for the diseases. If an oral glucose tolerance test (OGTT) was made in adults over 29 years of age, the prevalence could increase up to 10%.⁴ This would represent 2.5 million diabetics, with an annual increase in incidence by up to 3%-5%.⁵ In some communities, such as

the Canary Islands, the prevalence of DM2 has increased to almost 12%.⁶

TRENDS IN DM MORBIDITY AND MORTALITY

Spanish diabetic patients, both males and females, have a high mortality rate. According to data from the National Statistics Institute,⁷ 3,546 males and 5,686 females died from DM in 2000, but DM mortality should be higher considering that a substantial number of patients reported to die from cardiovascular or cerebrovascular causes or sudden death were undoubtedly diabetic.

The overall costs of diabetic patients have therefore increased in recent years. Mata et al. estimated DM costs at 2132 € per patient and year when microvascular and macrovascular complications exist.⁸

DOES THE DM «PANDEMIC» PERSIST?

In 2003, McKinlay et al.⁹ considered DM a real «epidemic».

A recent study by Lipscombe et al.¹⁰ compared changes in the incidence and prevalence of DM in the Ontario area, Canada, in the 1995-2005 period. Incidence increased by 69% and prevalence by 27%, while DM mortality decreased 25%.

Data reported by Wild et al. appear to suggest that the «epidemic» has not stopped, despite the increased monitoring and health education of the population.

What about kidney disease? Does the pandemic persist, or has DM stabilised as a cause of end-stage renal disease (ESRD)? An interesting and recent study by Friedman EA et al.¹¹ analysed the evolution of DM and diabetic nephropathy (DN) in the US between 1984 and 2003. New cases of DM were 16,000/year in 1984 and 43,000/year, with a peak of 46,000 patients/year in 1995. The rate of ESRD (KDOQI stage 5) was 250 pmp in 1984 and 230 pmp in 2003, with a peak incidence of 320 pmp in 1995.

According to these data, the incidence and prevalence of DM as a cause of advanced chronic kidney disease would be stabilising in the US.

DIABETIC NEPHROPATHY (DN) AND CHRONIC KIDNEY DISEASE (CKD) IN SPAIN

In parallel to the DM «plague», there has been an increase in the occurrence of KDOQI stage 5 ESRD as a result of DM.

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It has been reported for some years that 15% of patients with DM1 and 20%-40% of patients with DM2 will experience renal involvement during the course of diabetes depending on the multiple factors involved: genetic factors, glycemia control, adequate or inadequate blood pressure management, dyslipidemia, smoking, occurrence of microalbuminuria or progression to overt proteinuria, which will mark progression to established nephropathy.¹²

It has been estimated that more than 35% of DM2 patients in Spain have microalbuminuria, proteinuria, or CKD. If these data are extrapolated to the last population figures (45 million inhabitants), there could be more than one million diabetics with various grades of renal impairment. Diabetic patients have a 25-fold greater risk of experiencing renal failure as compared to the non-diabetic population.

The SEN Registry estimated in 1998 that diabetic patients accounted for 21% of all patients starting renal replacement therapy for KDOQI stage 5 CKD.¹³ The national figure given by the SEN Registry for 2004 was 23.3%,¹⁴ but wide differences existed between the autonomous communities. The lowest figures were found in La Rioja or the Basque Country, and the highest, 45% (76 patients per million inhabitants), was reported for the Canary Islands.^{15,16}

The MERENA study conducted by the GEENDIAB (Spanish group for the study of diabetic nephropathy) compared morbidity and mortality data for 1129 patients distributed into two cohorts, diabetics (n = 461) and non-diabetics (n = 668) in KDOQI stages 3 and 4.

Baseline study data showed diabetic patients in the study to be older and to have greater cardiovascular morbidity (dyslipidemia, ischaemic heart disease, heart failure, or peripheral vascular disease) as compared to the non-diabetic population.¹⁷

When mortality of this population was examined, the last unpublished data suggested that overall mortality of both populations after 3 years of follow-up was 12.6%. A higher mortality was seen in diabetic patients and particularly in KDOQI stage 4. Among the 456 patients ending the study at 3 years, 38% achieved the primary end-point due to starting renal replacement therapy, and 118 had died. Death occurred from cardiovascular causes in 49% of patients.¹⁸

GUIDELINES, CONSENSUS DOCUMENTS, AND PRACTICAL CLINICAL RECOMMENDATIONS

Plasma creatinine levels are not the ideal parameter to measure kidney function, particularly in diabetic patients. This is why the glomerular filtration rate is currently estimated using formulas, of which the most commonly used are the Cockcroft and Gault formula¹⁹ or the so-called MDRD formulas (derived from the Modification of Diet in Renal Disease study).²⁰

The Spanish consensus document established in 1997²¹ and modified in 2002²² standards that would serve as guidelines for detection and management of diabetic patients with nephropathy. This document was initially agreed by four scientific societies, and subsequently endorsed by three additional so-

cieties in 2002, which gives an idea of its importance. The document established criteria for detection of nephropathy at both an early stage (in the microalbuminuria stage both in DM1 and DM2) and more advanced stages of established nephropathy, and standards for comprehensive patient management (including cardiovascular risk factors) from primary to specialised care.

A common problem in daily clinical practice is identification of patients with CKD. Hidden or «undiagnosed» CKD is very common in our population, as shown by data from various studies, including EPIRCE,²³ EROCAP,²⁴ and DIREOC.²⁵ These studies demonstrate that CKD is more common in the diabetic population.

Various approaches have been used to attempt early identification of these populations in primary care in order to decrease comorbidity, particularly the comorbid CV conditions so common in diabetic and CKD patients.

The SEN, in collaboration with the Spanish Society of Clinical Chemistry (SEQC), prepared a consensus document to establish GFR estimation and thus apply the standards for early detection of CKD in primary care.²⁶

Other initiatives to optimise the cooperation between primary care and nephrology have been implemented throughout Spain, and a new consensus document has been agreed very recently with one of the leading primary care societies, SEMFYC, for that same purpose.²⁷ We nephrologists cannot obviously manage the «avalanche» of patients in whom a GFR lower than 60 mL/min is detected, but we can contribute to the use of adequate criteria for patient referral to nephrology departments and units in the setting of a close collaboration between healthcare professionals. This is particularly essential in DM, because it is the leading cause of advanced CKD.

SPECIFIC ASPECTS OF CKD AND DN

Some initiatives in which primary care physicians and nephrologists collaborate are being particularly useful in various Spanish areas. An example is the close cooperation in the Valencian Community between the department of health, primary care, and nephrologists from the Dr. Peset Hospital, coordinated by JL Górriz.

The department of nephrology of the Puigvert Foundation in Barcelona developed a teaching initiative, coordinated by F. Calero, consisting of a periodic rotation programme through the department for PC physicians.

In health area 5 of the Madrid Community, the La Paz Hospital has established, under the coordination of F. de Alvaro, an on line programme allowing contact with the hospital from basic health areas using a predefined questionnaire, as well as consultation with an experienced nephrologist through the web.

A different approach was used in health area 5 Costa de Ponent, where the DIREOC study²⁵ was started in collaboration with PC centres to detect CKD in populations at risk over 65 years of age with DM, HBP, or associated CV risk factors.

Among the 112 patients detected, 36% were diabetics and 80% had KDOQI stage 4 CKD.

COMPREHENSIVE CARE STRATEGY FOR DIABETIC PATIENTS

The Spanish National Health System is implementing since 2006 a comprehensive care strategy for DM patients²⁸ based on five essential principles:

- 1) Healthy lifestyle in primary prevention.
- 2) Early diagnosis of DM.
- 3) Treatment, suitability and optimisation of patient follow-up.
- 4) Adequate management of complications and special situations, such as gestational DM.
- 5) Education, research, and innovation programme for healthcare staff.

STRATEGIES IN CKD AND DM. OBJECTIVES

Diabetic patient care should be multifactorial and multidisciplinary, because highly diverse factors are involved in the occurrence and progress of DN and CKD in diabetic patients and many healthcare professionals are involved in comprehensive management of such patients.

In 2003, Gäede et al.²⁹ already emphasised that intensive, multidisciplinary care for patients with DM2 significantly decreased complications of diabetic microangiopathy and macroangiopathy as compared to patients receiving standard care.

This same group recently reported at the ASN-Renal Week, held in San Francisco in October-November 2007,³⁰ on follow-up of the 160 patients enrolled in that study. One hundred and thirty of those patients survived after a mean follow-up of 13.3 years. Patients receiving intensive and multidisciplinary care show reductions of 59% in the relative risk of CV events and 57% in mortality, and a much lower progression rate to KDOQI stage 5 CKD (occurring in 1 patient in the «intensive» group as compared to 6 patients undergoing standard care, $p = 0.037$).

The various studies available show a gradual increase in the number of CKD patients who require renal replacement therapy worldwide. This increase has been estimated at 7%-17%. It is obvious that such an increase causes a number of logistic and strategic problems that go beyond financial and social costs of DM for society, and that we nephrologists will not be able to meet the demand already existing.

Only when we become fully aware of the aspects of comprehensive education to patients and healthcare professionals involved in their care we will be able to stop the avalanche of CKD in diabetic patients.

Taking into account all issues discussed here, SEN and GEENDIAB intend to make a practical contribution to awareness of comprehensive management of diabetic patients and their cardiovascular risk. We think that it is very important to continuously update knowledge about management of diabetic patients in the light of the last advances in diag-

nosis and treatment, and also in application of any emerging new criteria.

We therefore intend to organise a course for continued nephrology training that will address epidemiological aspects, management of risk factors (high blood pressure, proteinuria, dyslipidemia, smoking, etc.), comprehensive management of diabetic patients with progressive CKD, and the time for considering treatment using dialysis and kidney or kidney and pancreas transplantation. This incoming course will be coordinated by Dr. Andrés Purroy.

REFERENCES

1. Wild S, Roglic G, Green A, Kng H. Global prevalence of Diabetes. Estimates for the year 2000 and projections for 2030. *Diab Care* 2004; 27 (5): 1047-1053.
2. Valdés S, Rojo-Martínez G, Soriguer F. Evolución de la prevalencia de la diabetes tipo 2 en población adulta española. *Med Clin (Barc)* 2007; 129 (18): 716-717.
3. Rodríguez Panós B, Sanchos C, García Gosálvez F, Divisón JA, Artigao LM, López Abril J, Naharro F, Puras A. The prevalence of diabetes mellitus and its association with other cardiovascular risk factors in the province of Albacete. The vascular disease Group of Albacete (GEVA). *Atención Primaria* 2000; 125: 166-171.
4. Castell C, Treserras R, Serra T, Goday A, Lloveras G, Sellares L. Prevalence of diabetes in Catalonia (Spain): an oral glucose tolerance test-based population study. *Diab Res Clin Metab* 1999; 43 (1): 33-40.
5. Goday A. Epidemiología de la diabetes y sus complicaciones no coronarias. *Rev Esp Cardiol* 2000; 55: 234-241.
6. De Pablos Velasco PL, Rodríguez-Pérez F, Pérez-Moreno JE, Anía-Lafuente B et al. Prevalencia de la diabetes mellitus no dependiente de insulina en Santa María de Guía. Estudios sobre diabetes mellitus en Canarias. Serie Epidemiológica. Servicio canario de salud, 1999.
7. Informe Instituto Nacional de Estadística 2000.
8. Mata M, Antoñanzas F, Tafalla M, Sanz P. The cost of type 2 diabetes in Spain: the CODE-2 study. *Gac Sanit* 2002; 16: 511-520.
9. McKinlay J, Marceasu L. US public health and the 21st century: diabetes mellitus. *Lancet* 2000; 356: 757-761.
10. Lipscombe L, Hux JE. Trends in diabetes, prevalence, incidence and mortality in Ontario, Canada 1995-2005: a population-based study. *Lancet* 2007; 369: 750-756.
11. Friedman EA, Friedman AL, Eggers P. End-stage renal disease in diabetic persons: is the pandemic subsiding? *Kidney Int* 2006; 70 (Supl. 104): s51-s54.
12. Martínez-Castelao A, De Álvaro F, Górriz JL. Epidemiology of diabetic nephropathy in Spain. *Kidney Int* 2005; 99 (Supl. Dec.): s20-s24.
13. García López F, Robles R, Gentil MA, Lorenzo Sellarés V, Clèries M, Escayola M, García Blasco MJ, Arrieta Lezama J, en representación del Grupo de Registros de Enfermos Renales de España: comparación de la incidencia, prevalencia, modalidad de tratamiento y mortalidad en pacientes con tratamiento renal sustitutivo en cinco comunidades autónomas españolas en el período 1991-1996. *Nefrología* 1999; 19: 443-459.
14. Arrieta J, Castro P, Gutiérrez Ávila G, Moreno Alía I, Sierra T, Estébanez C et al. Diálisis and Transplant situation in Spain 2004. *Nefrología* 2007; 27 (3): 279-299.
15. Lorenzo V, Martín-Urcuyo R. Análisis epidemiológico del incremento de insuficiencia renal asociada a diabetes mellitus tipo 2. *Nefrología* 2000; 20 (Supl. 5): 77-81.
16. Maceira B, López Alba A (coordinadores). ¿Quiénes son y dónde están las persona con diabetes en Canarias? PAD (Plataforma Ciudadana de Atención a la Diabetes). La Laguna (Canarias), 2004.
17. Martínez Castelao A, Górriz JL, De Álvaro F, Cases A, Luño J, Navarro J, Portolés JM. Morbidity and mortality factors in chronic renal disease in diabetic and non-diabetic patients (MERENA study). *JASN* 2004; 324A.

18. Martínez-Castelao A on behalf of the Cientific committee of the MERENA Study. VI Internacional Conference on Hypertension & the Kidney. Madrid, 28-29 February-1 March 2008.
19. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16: 31-41.
20. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal disease Study group. *Ann Inretn Med* 1999; 130: 461-470.
21. Documento de consenso sobre prevención y tratamiento de la Nefropatía Diabética en España. SEN, SEEN, SED y SEMFYC. *Nefrología* 1997; 17 (6): 467-474.
22. Documento de Consenso sobre detección, prevención y tratamiento de la nefropatía diabética en España. Asociación Española de Nefrología Pediátrica; Sociedad Española de Diabetes; SE Endocrinología y Nutrición; SE Hipertensión-LELHA; SEMFYC; SEMERGEN; SE Nefrología. *Nefrología* 2002; 22 (6): 521-530.
23. Otero A, Ganoso P, García F, De Francisco ALM, on behalf of the EPIRCE study group: epidemiology of chronic renal disease in the Galician population: results of the pilot Spanish EPIRCE study. *Kidney Int* 2005; 99 (Supl. Dec.): s16-s19.
24. De Francisco ALM, De la Cruz JJ, Cases A, De la Figuera M, Egocheaga MI, Górriz JL, Llisterri JL, Marín R, Martínez-Castelao A. Prevalencia de Insuficiencia renal en Centros de Atención Primaria en España: Estudio EROCAP. *Nefrología* 2007; 27 (3): 300-312.
25. Martínez-Castelao A, Bestard O, Moreso F, Soler M, García-Bayo I, López F, Fulladosa X, Duarte V, Grinyó JM. Detection of unknown Chronic Kidney Disease in elderly special populations (DIREOC Study). *J Am Soc Nephrol* 2006; 17: 147A.
26. Recommendations for the use of equations to estimate glomerular filtration rate in adults. Spanish Society of Nephrology. *Nefrología* 2006; 26 (6): 658-665.
27. Documento de consenso SEN-SEMFYC sobre Enfermedad Renal Crónica. <http://www.senefro@senefro.org/>
28. Plan Nacional de Salud e Investigación en Diabetes Mellitus 2006. Ministerio de Sanidad.
29. Gaede P, Vedel P, Larsen N, Jensen HV, Parving HH, Pedersen O: Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003; 348 (5): 534-542.
30. Gaede P, Parking HH, Pedersen O. Multifactorial intervention inpatients with type-2 diabetes: long-term effects on mortality and vascular complications. *J Am Soc Nephrol* 2007; 18: 43A.