© Med Sci Monit, 2004; 10(5): CR185-190
PMID: 15114267

CR

Received: 2003.01.10
Accepted: 2003.09.25
Published: 2004.05.01

Type 1 diabetes mellitus in Catalonia: chronic complications and metabolic control ten years after onset

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Ana Cantón[1], Miquel Fernández Castañer[1], Ignacio Conget[1], Gemma Carreras[1], Conxa Castell[2], Ricard Tresserras[2]

[1] Associació Catalana de Diabetis (ACD), Spain
[2] Consell Assesor sobre la Diabetis a Catalunya (CADC), Direcció General de Salut Publica, Departament de Sanitat i Seguretat Social, Generalitat de Catalunya, Spain

Source of support: This study was supported by a grant from the Catalan Diabetes Association, kindly sponsored by Lilly, S.A.

Summary

Background: The purpose of this article is to describe the prevalence of microvascular (retinopathy, nephropathy and neuropathy) and acute diabetic complications, and the metabolic control status, in Catalonian patients with type 1 diabetes mellitus ten years after diagnosis.

Material/Methods: We performed a cross-sectional population study evaluating 427 Type 1 diabetic patients diagnosed between 1987 and 1988 in 15 hospitals in Catalonia. 278 subjects were located, and all the study parameters were collected from their hospital medical records. Mean age at onset was 13.8±6.9 years, and 56.5% were male. The mean age of the patients was 24.8±6.7 years. Albumin excretion rate (AER), plasma creatinine, lipid profile, glycosilated hemoglobin (HbA_{1c}), blood pressure, presence of retinopathy and clinical polyneuropathy, and diabetes control were evaluated.

Results: The mean HbA_{1c} was 7.8±1.7%. HbA_{1c} was <7.5% in 48% of patients and >10% in 11.5%. The prevalence of retinopathy was 7.6%. An AER higher than 20 μg/min was found in 10.4%. Neuropathy was present in 4.3%. A significant association between microvascular complications as a whole (retinopathy and/or microalbuminuria and/or clinical polyneuropathy) and HbA_{1c} ($p=0.04$) and hypertension ($p=0.04$) was observed. There were no differences in diabetic complications regarding sex or age at presentation.

Conclusions: This is one of the first studies in which the prevalence of diabetic microvascular complications is reported in a South European cohort of subjects registered in EURODIAB. This population-based study confirms that complications are already present ten years after diabetes onset in a non-negligible percentage of patients.

key words: **type 1 diabetes mellitus • epidemiology • diabetic retinopathy • microalbuminuria • metabolic control**

Abbreviations: **MODY –** maturity onset diabetes of the young

Full-text PDF: http://www.MedSciMonit.com/pub/vol_10/no_5/3215.pdf

Word count: 2875
Tables: 1
Figures: –
References: 29

Author's address: Ana Cantón Blanco, Endocrinology Department, Hospital Universitari Germans Trias i Pujol, Ctra. de Canyet, s/n, 08916 Badalona, Spain, e-mail: acanton@ns.hugtip.scs.es

BACKGROUND

Epidemiological evidence suggests that environmental conditions and genetic factors can affect susceptibility to diabetic complications [1]. The great majority of patients with type 1 diabetes mellitus can expect to develop retinopathy [2], but only about 30% are at risk for nephropathy [3]. Diabetes duration and glycemic control are determining factors in the appearance of these complications [4–6], although other factors could possibly have a role [7]. Studying patients within a particular geographical area presents the opportunity to identify any regional differences which might give clues to environmental or other risk factors for the development of diabetic complications. Given that extrapolation of the results obtained in other countries may lead to significant health care mistakes, the determination of the prevalence of diabetic complications and associated risk factors in a defined geographic area is of importance in planning a well-coordinated approach to this public health problem.

The aim of our study was to describe the clinical situation in terms of prevalence of microvascular (nephropathy, retinopathy and clinical polyneuropathy) and acute diabetic complications, and metabolic control and associated risk factors, in patients included in the Catalan type 1 diabetes mellitus registry in 1987 and 1988, ten years after diagnosis of diabetes. This registry, initiated in Catalonia in 1987 to accurately and prospectively document the incidence of type 1 diabetes mellitus for individuals under the age of 30 years at diagnosis [8], joined the EURODIAB European collaborative program in 1989.

MATERIAL AND METHODS

The patients included in this study, all under the age of 30 at diagnosis, were those entered in the type 1 diabetes mellitus registry between 1 January 1987 and 31 December 1988. Catalonia is an Autonomous Community of Spain, with 6000,000 inhabitants, located on the Mediterranean coast, in the northeastern part of the Iberian peninsula. It is a geographically and demographically well-defined region, with an independent health service, where notification of diabetes is known to be about 90% [8].

All the patients had to be living in this region for at least 6 months prior to the diagnosis in order to be entered in the registry. Diabetes was defined according to the World Health Organization criteria [9]. Type 1 diabetes was defined by the presence of ketonuria and the necessity for permanent insulin therapy. All reported cases were on insulin treatment. The date of the first insulin injection was used as the date of inclusion in the study. Secondary diabetes and maturity onset diabetes of the young (MODY) were excluded.

The primary source of data was a contact system with all hospital endocrinology, diabetes and pediatric centers that reported diabetic patients to the registry during 1987 and 1988. Each center was provided with a list of patients entered by them during this period, in order to check which ones had reported to the diabetes clinic at least once during the previous 12 months. Some patients who were not registered in the clinic were contacted by telephone in order to find out where they were registered for follow-up at the time. All centers who might be treating type 1 diabetic patients in Catalonia were included in a mass mailing with the names of all the patients who could not be traced.

All data were obtained by the same person on the basis of a review of the hospital medical records of the individual patients, which entailed visiting all the participating centers. Each patient was given a personal identification code. The following data were collected: date of birth, sex, age (defined as the age at the time of the review of the medical records), age and date of clinical diagnosis (first insulin injection), number of consultations in the center and number of inpatient hospitalization in the last calendar year, glycosylated hemoglobin (HbA_{1c}), presence of microalbuminuria, presence of retinopathy and clinical polyneuropathy, cigarette smoking, systolic and diastolic blood pressure measures in the last 12 months, lipid profile (serum total cholesterol, HDL and LDL cholesterol, and fasting triglycerydes), frequency of blood glucose self monitoring, insulin schedule, and acute metabolic complications (severe hypoglycemia, ketosis and ketoacidosis) in the last year. Any episode severe enough to require the help of another person, including episodes of seizure and/or coma, was considered severe hypoglycemia. Ketoacidosis was defined as severe hyperglycemia and ketonuria with venous blood pH <7.25.

The albumin excretion rate (AER) was calculated from the 24 h urine collection, and was considered positive when two out of three consecutive determinations were pathological, in the absence of urinary infection. AER was defined as normal below 20 μg/min and elevated at or above this level. Microalbuminuria was defined as AER above 20 μg/min and less than 200 μg/min, and macroalbuminuria as above 200 μg/min. If plasma creatinine was >1.4 mg/dl on two occasions, this was considered indicative of renal failure.

The prevalence of retinopathy was calculated on the basis of examinations performed by an ophthalmologist, as stated in the medical records. Three different levels of retinopathy were defined: no retinopathy, non-proliferative retinopathy, and proliferative retinopathy.

The prevalence of neuropathy was established according to the guidelines of the San Antonio Conference on Diabetic Neuropathy [10]: the presence of compatible symptoms or signs in the setting of pathological clinical examination when other potential etiologies had been excluded.

The mean HbA_{1c} was calculated from all available measurements in each subject in the last 12 months. Since 15 centers were participating in the study, each one having a different HbA_{1c} normal range, a procedure to correct the differences was performed. The means and

standard deviations of local laboratories were used, and the control level was assessed in terms of standard deviation from the local laboratory mean, according to the formula:
[personal value-mean local value]/SD local value = number of SD

HbA_{1c} corrected values were calculated based on the pooled mean and standard deviation of all local laboratory values, according to the formula:
mean pooled + (SD pooled × number of SD) = corrected HbA_{1c} [11].

Those having systolic blood pressure ⩾130 mmHg or diastolic blood pressure ⩾85 mmHg, or under antihypertensive treatment, were considered hypertensive.

Current smokers (daily and occasional) were classified according to World Health Organization criteria [12]. This risk factor was analyzed only in those patients older than 14 at diagnosis.

Patients were considered to be doing self-monitoring of blood glucose if they performed at least one test per day.

Data were analyzed using the SPSS + PC for Windows statistical software program. Descriptive results are presented as proportions, with their 95% confidence limits in the case of a qualitative variable. If a quantitative variable is described, its mean value and standard deviation is presented.

When looking for association of complications (microalbuminuria, retinopathy, and clinical polyneuropathy as dichotomic variables) with other independent variables, *chi*-squared -test and Student's *t*-test or Mann-Whitney *U*-test (if distribution was not normal) were used, both for qualitative and quantitative variables. The level of statistical significance was assumed to be $p<0.05$.

RESULTS

The patient characteristics are given in Table 1.

Of an initial sample of 427 patients, 278 (65.1%) were located and had all medical data needed for the purposes of the study. The rest were not located (6.2%, n=30) or the data were insufficient (27%, n=111). Differences in age at onset (13.8±6.9 vs. 15.08±6.7 years) and sex (male/female, 56.5%/43.5% vs. 62.9%/37.1%) did not reach statistical significance between the group with complete information and the rest of the patients (not located or with insufficient data), $t=1.95$; $p>0.05$ and $\chi^2=1.59$, $p>0.05$, respectively. Patients with secondary diabetes and maturity onset diabetes of the young (MODY) were excluded (0.9%, n=4). Four patients (0.9%) had died, all from causes not related to diabetes.

The mean HbA_{1c} level for the whole studied population was 7.9±1.6% (range: 4.1–14.7), and the corrected mean value was 7.8±1.7% (range: 4.9–13.7); 128 patients (48%) were <7.5% and 32 (11.5%) were >10%.

Table 1. Characteristics of the patients.

N	278
Sex (male/female)	56.5%/43.5% (n=157/121)
Age at diabetes onset (years)	13.8±6.8
Clinical presentation at onset (%)	
• ketoacidosis	33.8 (n=94)
• ketosis	42.5 (n=118)
• hyperglycemia	23.7 (n=66)
Age at examination (years)	24.8±6.7
Weight (kg)/height (cm) at examination	65.5±11.2/166.7±11.4
Blood pressure (mm Hg)	
systolic	119.6±13.5
diastolic	70.1±9.9
Blood glucose monitoring (%)	89.6 (n=249)
Insulin injections per day (%)	
• two	19.4 (n=54)
• three	68.7 (n=191)
• four	11.9 (n=33)
HbA_{1c} (%)	7.8±1.7
Total cholesterol (mg/dl)	182.6±35.6
HDL cholesterol (mg/dl)	58.0±14.5
LDL cholesterol (mg/dl)	109.1±31.3
Fasting triglycerides (mg/dl)	70.4±47.7
Serum creatinine (mg/dl)	0.8±0.3
Microalbuminuria (%)	10.4 (n=29)
Retinopathy (%)	
• non proliferative	6.9 (n=19)
• proliferative	0.7 (n=2)
Hypertension (%)	20.4 (n=56)
Active smokers (%)	33.2 (n=92)
Number of consultations, preceding year	3.1±1.8
Severe hypoglycemia, preceding year	5.2 (n=14)

Data are mean ±SD or percentatge

In terms of chronic complications, non-proliferative retinopathy was found in 6.9% of the patients (n=19), and proliferative retinopathy in 0.7% (n=2), with no significant difference in the frequency of any retinopathy between men and women. No association was found between the presence of retinopathy, smoking habits, diastolic or systolic blood pressure, or hypertension. The mean HbA_{1c} was significantly higher in patients who developed retinopathy than in those who did not (8.8% vs 7.8%; $p=0.02$).

Microalbuminuria was observed in 10.4% of patients (n=29). The mean AER was 54.6±34.3 μg/min (range: 22.2–150). No patient with macroalbuminuria or renal insufficiency was found. The mean serum creatinine was 0.83±0.27 mg/dl. In our patient population, serum LDL cholesterol concentration was significantly higher (127.4 mg/dl vs. 107.4 mg/dl; $p=0.02$) and HDL concentration significantly lower (53.1 mg/l vs. 58.5 mg/dl; $p=0.04$) in patients with microalbuminuria than in those without, and this was the case in both sexes. The patients in the microalbuminuric group did not have significantly higher mean systolic and diastolic blood pressure or HbA_{1c} compared to the nonalbuminuric group. Nevertheless, those with microalbuminuria were more frequently hypertensive ($p=0.02$) and smokers ($p=0.02$).

Clinical polyneuropathy was present in 4.3% of patients (n=12). No association with age at onset, sex, blood pressure or hypertension was observed. An association was found between clinical polyneuropathy and HbA_{1c} (p=0.03) and smoking (p<0.05).

When the presence of microvascular complications was considered as a whole, retinopathy and/or microalbuminuria and/or clinical polyneuropathy, an association was found with HbA_{1c} (p=0.04) and hypertension (p=0.04). There were no differences in diabetic complications in terms of sex or age at presentation. No association with smoking was observed (p=0.06).

Regarding acute complications, only 1.5 % of patients (n=4) had experienced ketoacidosis during the 12-month period before the study. The prevalence of severe hypoglycemia in the last 12 months, including multiple episodes in some patients, was 5.2% (n=14). The percentage of one or more hospital admissions was 10.9% (n=30), the optimization of metabolic control being the most frequent cause of admission: 44.4% of cases (n=12).

Discussion

This study contributes to our knowledge of the prevalence of diabetic complications and metabolic control in type 1 diabetes mellitus in a region of Southern Europe, and confirms that complications are already present ten years after diagnosis in some subjects. The patients described herein are those in regular follow-up by specialized teams. As previously stated, 65.1% of the patients were located and had all medical data needed for the purposes of the study. The rest were not located (6.2%) or the data were insufficient (27%). This group of patients (not located or with insufficient data) correspond mainly to subjects followed by private practice, Primary Health Care, or under irregular follow-up. However, they were not different in terms of age, sex and age at onset in comparison to those who were followed up. For these reasons, although this is a limitation in some kind of poblational studies, we think that our data could be considered representative of this population, taking into account the handicap described.

There is a paucity of information about the prevalence of retinopathy in IDDM in Spain. Some reports refer to diabetic patients as a whole, not only type 1 diabetes [13]. The present study has revealed a relatively low prevalence of non-proliferative and proliferative diabetic retinopathy. The EURODIAB IDDM complications study on 3250 patients in Europe found that proliferative retinopathy was virtually absent before 10 years [14], and our results are generally consistent with this observation. Our results are similar to those of some studies [15,16] but much lower than those of others [2,17–19]. Patients with retinopathy had higher HbA_{1c} as it has previously been reported [14,15,17]. We used only the mean of determinations of HbA_{1c} performed in the last calendar year; in that case, the value of the analysis of the relationship between glycemic control and the prevalence of complications is limited. We think, however, that it probably reflects the metabolic control for a particular patient during a longer period. In this sense, Aghard et al. [20], in a 5-year follow-up study of 442 adult type 1 diabetic patients under routine care, showed that the individual levels of glycemic control and blood pressure can be kept fairly constant, the intraindividual coefficient of variation for HbA_{1c} values being 11±4%.

One patient out of ten had microalbuminuria. The diagnosis of patients in this phase of nephropathy is of great importance, given the high risk for developing established kidney disease and the possibility of treatment to avoid this progression [21]. The prevalence of microalbuminuria in our group is similar to that of previous reports [15,16,18]. Our prevalence is lower than that reported by some authors [2,22].

In a recent study on renal involvement in a representative sample of type 1 diabetes mellitus patients in Spain (n=1800 patients), 383 individuals out of all the patients studied had an evolution of diabetes of <5 years, with an 8.3% presenting microalbuminuria [23]. When analyzing patients with microalbuminuria in the whole sample vs those with normoalbuminuria, a statistically significant association was found with smoking, HbA_{1c} and diastolic blood pressure. We found an association between microalbuminuria and current smoking, and hypertension. The association between HbA_{1c} and the presence of microalbuminuria did not reach the level of statistical significance. Although several authors have reported an association between microalbuminuria and blood pressure [15–17], we could find no such association. No patient with macroalbuminuria or renal insufficiency was found, probably due to the relatively brief duration of type 1 diabetes in our group. Other studies reported a higher prevalence in patients also diagnosed at <30 years of age [24].

We found a statistically significant increase of LDL and a decrease of HDL cholesterol in patients with microalbuminuria in comparison to patients without. These results are consistent with those described previously [25], suggesting that patients who develop microalbuminuria have a worse lipid profile.

In our study, the prevalence of clinical polyneuropathy was 4.3% (n=12) with no difference according to sex. In a previous Spanish study of 2644 diabetic patients, recruited from primary health care centers and hospital clinics in 14 of the 17 Spanish Autonomous Communities, 13.2% had type 1 diabetes mellitus. Their mean age was 30.5±0.6 and the duration of diabetes (years) was 13.8±0.5, while the prevalence of neuropathy came to 12.9% (9.4–16.5) [26]. The discrepancy between the percentages of prevalence in these two studies is probably due to the slightly higher duration of diabetes in this group, although some other factors could be involved, including some methodological issues.

It should be borne in mind that the information provided by our work related to diabetic complications in type 1 diabetic patients would be more complete if we had evaluated them after one, two, or three years after disease onset. However, the work was initially designed as

a cross-sectional population-based study, not a follow-up study. We believe that this is an interesting point to be considered in the future, and, in fact, the results of this work will provide the basis for a prospective study of our population in which the incidence of diabetic complications and the pathogenic role of different risk factors will be determined.

The Sixth Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure (JNC-VI) recommended that pharmacological intervention be considered in those with diabetes who have blood pressure persistently ⩾130 mm Hg systolic or ⩾85 mmHg diastolic [27]. Using this cut-off level in our study, 20.4% of patients were hypertensive. The EURODIAB IDDM Complications Study examining 3250 randomly selected Type 1 diabetic patients with a mean duration of diabetes of 14.7±9.3 reported that 24% of subjects had hypertension, where the cut-off level was 140/90 or current use of antihypertensives [28].

In relation to metabolic control, our patients had lower HbA_{1c} than other groups [15,17,18]. This could be explained by the younger age of the patients included in those studies, with a higher percentage of children and adolescents, in whom metabolic control is more difficult.

The results presented herein are quite similar to the data reported by Esmatjes et al. [29]. This could be due to the fact that the sample of patients come out from the same population of type 1 diabetic patients.

CONCLUSIONS

We evaluated the prevalence of microvascular complications and level of metabolic control in patients with type 1 diabetes mellitus 10 years after diagnosis. We found that 7.6% have diabetic retinopathy, 10.4% microalbuminuria and 4.3% clinical polyneuropathy. The mean HbA_{1c} was 7.8±1.7%. Focusing research on the identification of associated risk factors could help us to prevent, or at least delay, the incidence of diabetic complications.

Acknowledgments

The authors are grateful to Ms. Nuria de Lara for her valuable work in processing the data base of the Catalan Registry of Diabetes, and to Ms. Eulalia Roure for her excellent work in the statistical analysis of data. We also want to thank Dr. A. Goday for his permanent contribution to the Catalan Registry. The authors are especially grateful to Dr.G.Lloveras, president of the Advisory Committee on Diabetes Mellitus in Catalonia, from the Department of Health of the Autonomous Government, for his support and constant stimulus. We are indebted to professionals and centers contributing to the Catalan Diabetes Registry. This work would not have been possible without their participation.

Centers and responsible parties

I. Conget (Hospital Clinic i Universitari, Barcelona); M. Fernández-Castañer (Hospital Bellvitge, Hospitalet Llobregat); A. Pérez, G. Carreras (Hospital Sant Pau, Barcelona); F. Cano (Hospital del Mar, Barcelona); J. Rodriguez-Hierro (Hospital Sant Joan de Deu, Barcelona); C. Hernández, A. Cantón, E.Vicens Calvet (Hospital Vall d' Hebron, Barcelona); I. Salinas (Hospital Germans Trias i Pujol, Badalona); A. Palaudarias (Consorci Sanitari Mataró, Mataró); D. Mauricio (Hospital Parc Taulí, Sabadell); J. Anglada (Hospital de la Mútua de Terrasa, Terrassa); V. Yetano, I Castells (Hospital General de Granollers, Granollers); W. Ricart, J.Vidal (Hospital Josep Trueta, Girona); F.Rius (Hospital Arnau de Vilanova, Lleida); J.Vendrell (Hospital Joan XXIII, Tarragona); P.Sardá (Hospital San Joan, Reus).

Other collaborators who helped in tracing some of the patients

M. Aliart, D. Figuerola, M. Gussinyé, A. Gutiérrez, J.M. Mallafré, A. Mejías, L.Vila.

REFERENCES:

1. Marre M: Genetics and the prediction of complications in type I diabetes. Diabetes Care, 1999; 22: B53-B58
2. Orchard TJ, Dorman JS, Maser RE et al: Prevalence of complications in IDDM by sex and duration. Pittsburgh Epidemiology of Diabetes Complications Study II. Diabetes, 1990; 39: 1116-24
3. Andersen AR, Christiansen JS, Andersen JK et al: Diabetic nephropathy in type 1 (insulin-dependent) diabetes: an epidemiological study. Diabetologia, 1983; 25: 496-501
4. Krolewski AS, Warram JH, Rand LI, Kahn CR: Epidemiologic approach to the etiology of type 1 diabetes and its complications. N Engl J Med, 1978; 317: 1390-98
5. Wang PH, Lau J, Chalmers TC: Meta-analysis of effects of intensive blood-glucose control on late complications of type 1 diabetes. Lancet, 1993; 341: 1306-9
6. DCCT Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993; 329: 977-86
7. Karamanos B, Porta M, Songini M et al: Different risk factors of microangiopathy in patients with Type 1 diabetes mellitus of short versus long duration. The EURODIAB IDDM Complications Study. Diabetologia, 2000; 43: 348-55
8. Goday A, Castell C, Tresserras R et al: Incidence of type 1 (insulin-dependent) diabetes mellitus in Catalonia, Spain. The Catalan Epidemiology Diabetes Study Group. Diabetologia, 1992; 35: 267-71
9. Expert Committee on Diabetes Mellitus World Health Organization. WHO Technical report series 1980, ns 616
10. Consensus Statement Report and recommendations of the San Antonio Conference on Diabetic Neuropathy. Diabetes, 1988; 37: 1000-04
11. Armitage O, Berry G: Statistical methods in medical research. Blackwell Science, Oxford, 1995
12. World Health Organization: The Evaluation and Monitoring of Public Action on Tobacco. Smoke-free Europe: 3, Copenhagen, 1990
13. Fernández-Vigo J, Sanchez Macho J, Diaz Rey A et al: The prevalence of diabetic retinopathy in Northwest Spain. An epidemiological study of diabetic retinopathy in Galicia. I. Acta Ophthalmol (Copenh), 1993; 71: 22-6
14. Sjolie AK, Stephenson J, Aldington S et al: Retinopathy and vision loss in insulin-dependent diabetes in Europe. The EURODIAB IDDM Complications Study. Ophthalmology, 1997; 104: 252-60
15. Joner G, Brinchmann-Hansen O, Torres CG, Hanssen KF: A nationwide cross-sectional study of retinopathy and microalbuminuria in young Norwegian Type 1 (insulin-dependent) diabetic patients. Diabetologia, 1992; 35: 1049-54

16. Gomes MB, Lucchetti MR, Gazzola H et al: Microalbuminuria and associated clinical features among Brazilians with insulin dependent diabetes mellitus. Diabetes Res Clin Pract, 1997; 35: 143-47
17. Olsen BS, Johannesen J, Sjolie AK et al: Metabolic control and prevalence of microvascular complications in young Danish patients with Type 1 diabetes mellitus. Diabetic Med, 1999; 16: 79-85
18. Bognetti E, Calori G, Meschi F et al: Prevalence and correlations of early microvascular complications in young type 1 diabetic patients: role of puberty. J Pediatr Endocrinol Metab, 1997; 10: 587-92
19. Klein R, Klein BE, Moss SE et al: The Wisconsin epidemiologic study of diabetic retinopathy II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. Arch Ophthalmol, 1984; 102: 520-26
20. Agardh CD, Agardh E, Torffvit O: The association between retinopathy, nephropathy, cardiovascular disease and long-term metabolic control in type 1 diabetes mellitus: a 5 year follow-up study of 442 adult patients in routine care. Diabetes Res Clin Pract, 1997; 35: 113-21
21. Viberti G, Mogensen CE, Groop LC, Pauls JF: Effect of captopril on progression to clinical proteinuria in patients with insulin-dependent diabetes mellitus and microalbuminuria. JAMA, 1994; 271: 275-79
22. Stephenson JM, Fuller JH, Viberti GC et al, the EURODIAB IDDM Complications Study Group. Blood pressure, retinopathy and urinary albumin excretion in IDDM: the EURODIAB IDDM Complications Study. Diabetologia, 1995; 38: 599-603
23. Estudio Diamante. Renal involvement in type 1 (IDDM) diabetes in Spain. Diabetes Res Clin Pract, 1997; 38: 129-37
24. Klein R, Klein BE, Moss SE et al: The 10-year incidence of renal insufficiency in people with type 1 diabetes. Diabetes Care, 1999; 22: 743-51
25. The DCCT Research Group. Lipid and lipoprotein levels in patients with IDDM. Diabetes Care, 1992; 15: 886-94
26. J. Cabezas-Cerrato for the Neuropathy Spanish Study Group of the Spanish Diabetes Society (SDS). The prevalence of clinical polyneuropathy in Spain: a study in primary care and hospital clinic groups. Diabetologia, 1998; 41: 1263-69
27. The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. The Sixth Report. Arch Intern Med, 1997; 157: 2413-46
28. Collado-Mesa F, Colhount HM, Stevens LK et al: Prevalence and management of hypertension in type 1 diabetes mellitus in Europe: the EURODIAB IDDM Complications Study. Diabetic Med, 1999; 16: 41-48
29. Esmatjes E, Castell C, Goday A et al: Prevalencia de nefropatía en la diabetes mellitus tipo 1. Med Clin (Barc), 1998; 110: 6-10

Index Copernicus

Global Scientific Information Systems for Scientists by Scientists

TM
INDEX COPERNICUS INTERNATIONAL

www.IndexCopernicus.com

- EVALUATION & BENCHMARKING
- PROFILED INFORMATION
- NETWORKING & COOPERATION
- VIRTUAL RESEARCH GROUPS
- GRANTS
- PATENTS
- CLINICAL TRIALS
- JOBS
- STRATEGIC & FINANCIAL DECISIONS

Index Copernicus integrates

IC Scientists

Effective search tool for collaborators worldwide. Provides easy global networking for scientists. C.V.'s and dossiers on selected scientists available. Increase your professional visibility.

IC Virtual Research Groups [VRC]

Web-based complete research environment which enables researchers to work on one project from distant locations. VRG provides:

- customizable and individually self-tailored electronic research protocols and data capture tools,
- statistical analysis and report creation tools,
- profiled information on literature, publications, grants and patents related to the research project,
- administration tools.

IC Journal Master List

Scientific literature database, including abstracts, full text, and journal ranking. Instructions for authors available from selected journals.

IC Patents

Provides information on patent registration process, patent offices and other legal issues. Provides links to companies that may want to license or purchase a patent.

IC Grant Awareness

Need grant assistance? Step-by-step information on how to apply for a grant. Provides a list of grant institutions and their requirements.

IC Conferences

Effective search tool for worldwide medical conferences and local meetings.

IC Lab & Clinical Trial Register

Provides list of on-going laboratory or clinical trials, including research summaries and calls for co-investigators.