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ORIGINAL ARTICLE

Age and sex differences in the incidence of diabetes mellitus in a population-based Spanish cohort

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Abstract

Background: The prevalence of diabetes mellitus (DM) in Spain ranges between 10% and 20%. However, very little is known about the incidence of DM because of difficulties involved in estimating it and its apparent lack of usefulness in practice. The aim of the present study was to describe the incidence of type 1 and type 2 DM (T1DM and T2DM, respectively) in the Castilla y León diabetes cohort (CODICyL).

Methods: New diabetes cases, were registered on a standard form that included diagnostic criteria, background, symptoms, results of clinical examination, complications, other cardiovascular risk factors, and treatment. There were 1 354 619 person-years monitored between 2000 and 2013. We estimated the incidence of DM and calculated the relative risks adjusted for age, gender, and year of diagnosis with Poisson regression models.

Results: The incidence of DM in individuals aged ≥15 years was 196.9 per 100 000 person-years (95% confidence interval [CI] 188.4–205.7), whereas in those aged <15 years the incidence was 10.8 per 100 000 person-years (95% CI 7.8–14.8). Men had a 36% higher risk than women of developing T2DM (95% CI 25%–49%). The greatest incidence of T2DM was found in 55–64-year-old men and 65–69-year-old women.

Conclusions: The annual incidence of T2DM is approximately 2 per 1000 person-years, higher in men, and peaks in middle age. Although specific tests to differentiate between the two types of DM are not available in this study, the estimation of incidence in those <15 years of age (10.8 per 100 000 person-years) represents a close approximation of the incidence of T1DM.

Keywords: diabetes mellitus, epidemiology, incidence.

Significant findings of the study: Males are at a higher risk of developing diabetes at an earlier age than females. **What this study adds:** The results of the study are relevant for policy makers and for establishing guidelines for early diagnosis (age of onset). In addition, the results contribute to our understanding of the present burden of diabetes and the forecast for the disease (dynamics of the diabetes epidemic).

Introduction

Diabetes mellitus (DM) is one of the most common diseases, causing great cost in Western countries. The World Health Organization (WHO) has estimated that, in 2030, there will be 366 million people with diabetes worldwide and that the prevalence of DM at this time will reach 4.4%.[1]

The prevalence of DM in Spain and other European countries is well known and is in the range 10%–20% depending on the study population.[2–5] In the autonomous region of Castilla y León (Spain), a 2004 study on the risk of cardiovascular disease reported that the estimated prevalence of DM was 8.8% in the population aged >15 years.[6]

However, the incidence of DM remains relatively unknown because of the difficulties associated with its estimation and the limited epidemiological value given to it until now. In studies performed in several populations in Europe,[7] the annual incidence of type 2 DM (T2DM) generally ranges between 120 and 410 per 100 000 population. Prospective studies with a longer follow-up period have reported that, in general, the annual incidence in subjects with prior glucose regulation disorders falls between 2% and 5%.[8]

Incidence data for T2DM in Spain are considered partial, given that very few population studies have taken follow-up into account and the values are higher than those reported for other European countries. The Lejona study estimated an incidence rate of 8 per 1000 person-years,[9] whereas the most recent study performed in Asturias reported an incidence of 10.8 per 1000 person-years.[10]

One strategy that makes prospective follow-up of a patient cohort possible is the use of diabetes registries, many driven by the St. Vincent declaration in 1989.[11] However, most of the significant international cohorts, such as the UK Prospective Diabetes Study (UKPDS),[12] which recruited 5102 patients with T2DM in England, Northern Ireland, and Scotland in 1977, have not performed incidence estimations because reference populations were not available. The focus of these studies, which included follow-up periods >20 years in some cases, was to evaluate the effects of glycemic control protocols, the appearance of complications, and survival rates.

There are more incidence studies based on local registries for type 1 DM (T1DM). The most recent Spanish data estimate rates of 8.7 per 100 000 person-years in the community of Navarra for the period 2009–11,[13] and 15.9 per 100 000 person-years in the community of Madrid for the period 1997–2005.[14]

The aim of the present study was to determine the incidence of new DM diagnoses in the Castilla y León diabetes cohort (CODICyL).

Methods

The CODICyL

In 2000, the Castilla y León Health Sentinel Network (RCSCyL) began a registry of new diagnoses of diabetes to set up a regional cohort of patients (CODICyL).[15] The RCSCyL is a specific information system focused on vigilance in public health and epidemiological research in which some 300 health professionals voluntarily participate. There are seven different programs aimed at specific populations, and each year different health problems of interest on which the management committee agrees are registered. Between 140 and 150 primary care physicians and pediatricians participate in the CODICyL cohort program every year.

Each new diabetes diagnosis made in the population covered by sentinel physicians and pediatricians is noted on a form containing baseline information at diagnosis. The patient is then included in the CODICyL register for annual follow-up. Cases are added to this open cohort as they are diagnosed. For the present study, the inclusion of new cases ended on 31 December 2011.

For inclusion as newly diagnosed DM, subjects had to meet the 1997 criteria of the American Diabetes Association,[16] as follows: (i) random blood glucose levels ≥200 mg/dL along with classic diabetes symptoms (polydipsia, polyuria, polyphagia, and weight loss); (ii) fasting blood glucose ≥126 mg/dL on at least two occasions; (iii) glycemia at 2 h after oral overload with 75 g glucose (i.e. ≥200 mg/dL) on at least two occasions.

The data on the form included the biochemical parameters on which the diagnosis was based, which were checked and validated in the network coordinating center. In addition, information was collected regarding patient background, symptomatology, clinical examination, other cardiovascular risk factors, macro- and microvascular complications, and treatment.

The annual follow-ups consisted of systematic collection, using a standard form, of information regarding clinical and analytical data, complications, and treatments throughout the calendar year (1 January–31 December). Family doctors and patients' nurses provided this information from the data noted on the case history (paper or electronic) between February and March of the following year. The forms included retrospective patient information so that the sentinel physician could correct errors in previously collected data and verify the diabetic condition. Incident cases were introduced into a database designed especially for the study, which included various cohort control and follow-up routines and automation of the sending and receiving of information.

Reference population

The reference population for the incident cases was the population covered each year by the RCSCyL system: the regional health system assigns each person to one physician and pediatrician list. The age and sex of the people on the list were collected each year from the regional health databases. The sum of the population lists of each participant is the annual reference population.

Doctors that changed location continued reporting incident cases in the new list, and their annual reference population was calculated by weighting populations in both lists by the number of weeks of activity. The sum of reference populations for all years of follow-up is 1 354 619 person-years.

Data analysis

To estimate incidence, we chose a diagnoses of diabetes between 1 January 2000 and 31 December 2011. Registers of gestational diabetes were excluded. No strict distinction was made between T1DM and T2DM in the analysis of cases, given that there was no information available regarding specific tests on autoimmune changes, insulin resistance, or genetics. However, we performed estimations and analyses separating patients into those <15 years of age (exclusively T1DM) and those aged ≥15 years (mostly T2DM). We estimated the annual incidence rates per 100 000 inhabitants for the total period studied, per year, by age group and sex. Confidence intervals (CI) were calculated assuming a Poisson distribution.

Specific predicted rates by age and by year of diagnosis were calculated for males and females, adjusting a Poisson regression model with the variables age, sex, year of diagnosis, and the interaction between age and sex. Similarly, relative risks (RR) for the comparison of groups were estimated using Poisson regression models, adjusting by year of diagnosis, group age, and sex.

The joint database set up in MS Access (Microsoft Corporation, Redmond, WA, USA) was debugged and analyzed using SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

The 12-year period yielded 2010 new diabetic patients valid for inclusion in the present study. Of these, 57% were male and 43% were female; 38 were children (i.e. <15 years of age). Figure 1 shows diagnoses per year of registry and the total number of patients accumulated. In 2000 and 2002, more than 250 cases were included in the cohort annually, whereas the number of cases added was noticeably lower in the other years. This variation is reflected in the estimated rates per year, with a maximum of 241.5 and a minimum of 100.6 cases per 100 000 in 2002 and 2007, respectively (Table 1).

The mean annual incidence rate in the study period was estimated to be 148.4 cases. If only those aged ≥15 years (mainly T2DM) were considered, the rate was 196.9 (95% CI 188.4–205.7). For those aged <15 years (T1DM), the mean annual incidence rate was 10.8 (95% CI 7.8–14.8).

The incidence of diabetes according to age group and sex is given in Table 2. In patients aged ≥15 years, incidence was significantly ($P < 0.05$) greater among men (224.0 per 100 000; 95% CI 211.2–237.5), than among women (169.7 per 100 000; 95% CI 158.7–181.5). Incidence increased with age, with maxima in 55–64-year-old men and 65–69-year-old women; incidence dropped after these ages. The expected rates by age, year of diagnosis, and sex according to the Poisson regression model are

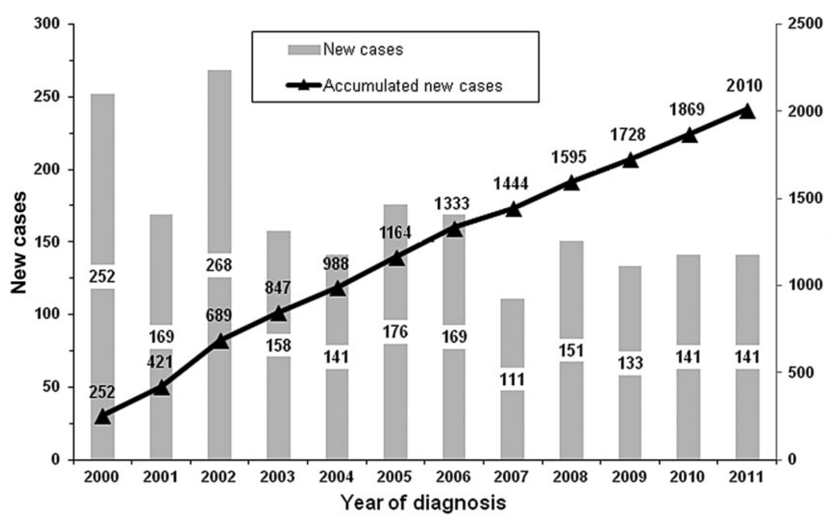

Figure 1 New and accumulated cases per year over the period 2000–11 in the Castilla y León diabetes cohort.

Table 1 Annual diabetes mellitus incidence rates per 100 000 person-years, according to type and year of diagnosis

	Reference population (in person-years)	Rate per 100 000	95% CI
Type			
15 years of age (T1DM)	352 902	10.8	7.8–14.8
≥15 years of age (T2DM)	1 001 717	196.9	188.4–205.7
Year of diagnosis			
2000	117 682	214.1	189.3–242.3
2001	117 579	143.7	123.6–167.1
2002	110 989	241.5	214.2–272.2
2003	116 975	135.1	115.6–157.9
2004	101 998	138.2	117.2–163.0
2005	116 101	151.6	130.8–175.7
2006	117 527	143.8	123.7–167.2
2007	110 336	100.6	83.5–121.2
2008	116 280	129.9	110.7–152.3
2009	109 212	121.8	102.7–144.3
2010	116 280	121.3	102.8–143.0
2011	103 661	136.0	115.3–160.4
Total	1 354 619	148.4	142.0–155.0

T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; CI, confidence interval.

Table 2 Annual diabetes mellitus incidence rates per 100 000 population according to age group and gender

	Total		Males		Females	
Age group (years)	Rate	95% CI	Rate	95% CI	Rate	95% CI
0–4	6.0	2.9–12.5	3.4	0.8–13.4	8.7	3.6–20.9
5–9	12.4	7.5–20.6	14.6	7.6–28.0	10.2	4.6–22.7
9–14	13.9	8.5–22.7	20.5	11.6–36.1	7.1	2.7–18.8
Total (<15 years)	10.8	7.8–14.8	12.8	8.5–19.2	8.7	5.2–14.4
15–19	7.5	2.8–20.1	11.0	3.5–34.0	3.9	0.5–27.6
20–24	6.3	2.4–16.8	8.9	2.9–27.6	3.4	0.5–24.0
25–29	11.9	6.2–22.8	15.1	6.8–33.7	8.3	2.7–25.8
30–34	19.9	12.2–32.4	28.6	16.2–50.4	10.4	3.9–27.6
35–39	45.8	33.3–62.9	62.8	43.0–91.5	27.5	15.2–49.7
40–44	98.6	79.4–122.5	124.9	95.7–163.1	70.2	48.4–101.6
45–49	181.1	153.4–213.9	244.2	200.8–297.1	108.9	79.6–149.1
50–54	278.3	241.0–321.3	354.3	297.8–421.7	190.4	147.5–245.7
55–59	380.0	335.0–431.1	495.6	425.2–577.5	255.0	204.3–318.4
60–64	446.9	396.5–503.8	499.5	426.1–585.6	392.7	327.4–471.1
65–69	448.8	400.0–503.4	471.0	401.3–552.7	427.3	362.3–504.0
70–74	389.9	347.1–437.9	437.3	372.8–512.9	347.1	292.8–411.4
75–79	319.0	278.8–364.9	336.4	276.8–408.8	304.6	252.9–366.9
80–84	283.7	240.2–335.0	265.3	203.7–345.5	297.2	240.0–368.0
85+	136.3	105.4–176.3	119.8	75.5–190.2	145.3	106.6–198.1
Total (≥15 years)	196.9	188.4–205.7	224.0	211.2–237.5	169.7	158.7–181.5

CI, confidence interval.

shown in Fig. S1, available as Supporting Information for this paper. There were no interactions between year of diagnosis and age.

With respect to the population <15 years of age, the incidence tended to be greater in males than females (12.8 per 100 000 [95% CI 8.5–19.2] vs 8.7 per 100 000 [95% CI 5.2–14.4], respectively), but the difference did not reach statistical significance ($P = 0.24$).

The RR for males compared with females, adjusted by age and year of diagnosis, with the Poisson regression model is 1.36 (95% CI 1.25–1.49) for those ≥15 years and 1.47 (95% CI 0.7–2.8) for those <15 years. Using the

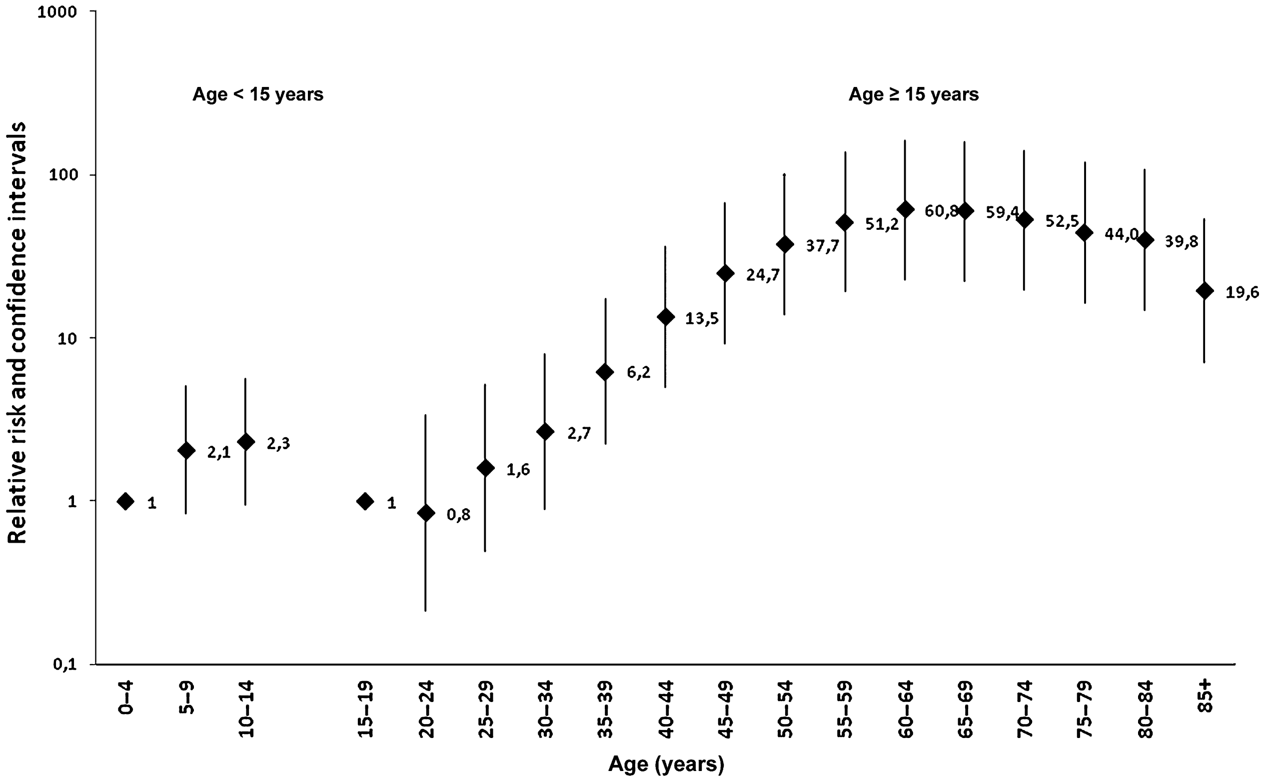

Figure 2 Relative risk according to age group, adjusted for sex and year of diagnosis using a Poisson regression model.

15–19-year-old age group as the reference for adult diabetes, RR increased with age. The risk started to become significant at 35–39 years of age, with an RR of 6.2 (95% CI 2.2–17.4), and peaked at 60–64 years of age, with an RR of 60.7 (95% CI 22.6–163.1; Fig. 2). For T1DM in those <15 years of age, the RRs for the 5–9 and 10–14 age groups compared with the 0–4 years group were 2.1 (95% CI 0.83–5.03) and 2.3 (95% CI 0.94–5.57), respectively ($P = 0.062$).

Discussion

In the present study, we calculated the incidence of DM according to age group, making it possible to estimate the incidence of diabetes in patients aged ≥15 years (mainly T2DM) and in those aged <15 years (T1DM).

The likelihood ratios to measure the effects of the three variables included in the regression model were significant ($P < 0.01$). The data confirmed a 36% higher ($P < 0.05$) incidence in men than women aged ≥15 years, which agrees with the literature.[17] This difference has also been reported for T1DM,[18] but was not significant in the present study because of the sample size.

Looking at the different age groups, it was evident that DM incidence peaks at around 65 years of age. The slightly higher incidence of DM in the 15–19 year age group compared with the 20–24 years age group may be due to the onset of diagnosis of T1DM in adolescents >14 years of age. From that age on, the increase is very notable and earlier in males than females, doubling the rates until almost 60–65 years old. The lower incidence at advanced ages may be related to the mean age of appearance and diagnosis of DM, but could also be related to the survival of individuals at lower risk of developing DM.

The number of cases registered each year varied. The higher rate in the first year of the registry could be explained as a consequence of over vigilance at the beginning of the study. There was also a significant increase in the number of cases reported in 2002, probably due to the registration of borderline cases from previous years before the application of the new diagnostic criteria published in 1997 by the ADA[16] and in 1999 by the WHO,[19] which were included in the regional guidelines beginning in 2000. From 2002 on, the incidence estimated in the CODICyL cohort remained stable for 10 years. The rates are consistent with rates published in the scientific literature for both T1DM in children and adolescents and for T2DM in the adult population.[7,13,14]

These data, although coming from a registry of a population sample, to which both sentinel primary care physicians and pediatricians contributed, have the added value of presenting the reality of diabetes in the health system across a wide region of Spain, which is the same in the rest of the country. Although in the majority of prevalence studies there is always a significant number of undiagnosed cases, the risk of underestimating the incidence in this case is reduced because the doctors involved in the sentinel network were trained and asked to identify all possible cases in their population in an active surveillance for a long period of time. Consequently, the newly diagnosed cases are considered a good approximation of the actual incidence of diabetes and could be extended to other regions for the study of population variations.

Incidence rates in Spain for the population <15 years of age range from 8.9 to 14.9 cases per 100 000 children.[20] Data from the Community of Madrid put the rate at approximately 16 per 100 000,[14] much higher than that found in the present study, but the most recent data from the region of Navarra reports an estimate of 8.7 per 100 000.[13] A possible explanation for these differences could be that some of the patients were diagnosed and controlled in specialized pediatric services or in endocrinology departments, which would lead to an underestimation of the rate.

With regard to T2DM, the Lejona study (in adults >30 years of age) found an incidence higher than the approximately 200 cases per 100 000 inhabitants estimated in Castilla y León.[9] Similarly, the Asturias study (in adults aged 30–75 years) reported a much higher incidence,[10] probably due to the methods used. Values slightly higher were found in a study on a Swedish community over 30 years,[21] with an incidence of 303 per 100 000 (although the reference population was also older, between 35 and 79 years of age, an age group in which the greatest number of cases are usually diagnosed). Similar estimates were reported by a retrospective study in Reykjavik,[22] which found an annual incidence of 337 per 100 000 for men and 266 per 100 000 for women.

One of the limitations of the present study is that findings from complementary tests on autoimmune destruction of pancreatic β-cells, insulin resistance, and genetics are unavailable. These tests would make it possible to differentiate clearly between T2DM, mature-onset DM in younger individuals and latent autoimmune diabetes in adults.[23]

The incidence rate is one of the lesser known diabetes indicators, but it is still relevant despite this. Differences in epidemiological patterns and changes over time are clearly directly related to the natural history of the condition, as well as having implications for models of prevention and early diagnosis. Although the CODICyL cohort was closed in 2012, an automated annual follow-up system was implemented using the registers of the Castilla y León electronic case history scheme; this follow-up system will make it possible to study the degree of control, incidence of complications, and survival in the future.

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Disclosure

The authors declare they have no conflicts of interest.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Figure S1 Incidence rates according age group and year in (a) males and (b) females, adjusted using a Poisson regression model.

