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ScienceDirect
Diabetes & Metabolism 34 (2008) 601–605
Diabetes & Metabolism
http://france.elsevier.com/direct/diabet

Original article

The growing incidence of type 1 diabetes in children: The 17-year French experience in Aquitaine

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Received 11 March 2008; received in revised form 28 May 2008; accepted 3 June 2008
Available online 25 October 2008

Abstract

Background. – While the incidence of type 1 diabetes in children has increased in various parts of the world, in France, no actual figures have been available since 1997.

Objective. – The aim of this study was to determine whether or not the pattern of increase in the incidence of type 1 diabetes in children aged less than 15 years varies with age at onset in Aquitaine (France) over a 17-year period.

Patients and methods. – From 1988 to 1997, all newly diagnosed cases of type 1 diabetes were confirmed by registration into the French Registry of Incidence of Diabetes. Subsequently, all cases registered from 1998 to 2004 were collected within paediatric centres in Aquitaine as part of their hospital-based prospective records.

Results. – In the overall population, the age- and gender-adjusted incidence rate increased from 8.86 per 100,000 per year (95% CI: 6.27–11.45) in 1988 to 13.47 per 100,000 per year (95% CI: 10.29–16.65) in 2004, indicating an annual increase in incidence of 3.34% (95% CI: 3.33–3.34). Median age at diabetes onset for cases in the first registration period (1988–1996) was significantly higher than that in the second registration period (1997–2004): 10.04 years (range: 6.64–12.53) versus 8.83 years (range: 5.48–11.73), respectively ($P = 0.01$). The annual increase in incidence rate was highest in the youngest children and varied significantly with age (0–4 years: 7.59%; 5–9 years: 4.06%; 10–14 years: 1.28%).

Conclusion. – These results indicate a doubling of the incidence of type 1 diabetes in children every 30 years in Aquitaine, with an even steeper increase among younger children, thus underscoring the need for appropriate adaptation of the system of healthcare provision.

Résumé

Augmentation continue de l'incidence du diabète de l'enfant : expérience française en Aquitaine sur 17 ans.

Justification. – Alors que l'accroissement de l'incidence du diabète de type 1 chez l'enfant a été rapporté en Europe, aucune donnée n'est plus disponible dans notre pays depuis 1997.

Objectifs. – Mesurer sur 17 ans, l'augmentation de l'incidence du diabète de type 1 découvert chez les enfants de moins de 15 ans en Aquitaine (France).

Patients et méthodes. – De 1988 à 1997, le recueil des nouveaux cas de diabète de type 1 a été réalisé au sein du Registre français d'incidence du diabète. De 1998 à 2004, le recueil a été fait à partir de l'enregistrement prospectif réalisé par tous les services de pédiatrie d'Aquitaine.

Résultats. – L'incidence ajustée sur l'âge et le sexe est passésde 8,86 pour 100 000 par an (intervalle de confiance [IC] 95 % : 6,27–11,45) en 1988 à 13,47 pour 100 000 par an (IC 95 % : 10,29–16,65) en 2004. Sur cette période, l'augmentation annuelle de l'incidence pour l'ensemble de la population était de 3,34 % (IC 95 % : 3,33–3,34). L'âge médian au diagnostic de diabète lors de la première période de recueil (1988–1996) était significativement plus élevé que celui de la deuxième période de recueil (1997–2004) : 10,04 (extrêmes : 6,64–12,53) versus 8,83 ans (extrêmes : 5,48–11,73 ; $P = 0{,}01$). Pendant ces 17 ans, l'augmentation annuelle de l'incidence était significativement plus élevée chez les enfants les plus jeunes (0–4 ans : 7,59 % ; 5–9 ans : 4,06 % ; 10–14 ans : 1,28 %).

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1262-3636/$ – see front matter © 2008 Published by Elsevier Masson SAS.
doi:10.1016/j.diabet.2008.06.002

Conclusions. – Ces résultats indiquent que l'incidence du diabète de type 1 chez l'enfant est en train de doubler tous les 30 ans et encore plus vite chez les tout-petits, ce qui doit conduire à renforcer l'offre de soins pour cette maladie si particulière à cet âge de la vie.

Keywords: Children; Type 1 diabetes mellitus; Incidence; Increase; Age group

Mots clés : Enfants/adolescents ; Diabète de type 1 ; Épidémiologie ; Incidence

1. Introduction

During the last few decades of the 20th century, an increase in the incidence of type 1 diabetes in children was reported in Europe as well as in most other parts of the world [1,2]. The reasons for this increase remain unclear, but it has been suggested that changes in environmental factors – mostly dietary and infectious – may be interacting with a genetic predisposition to promote a more aggressive form of autoimmune disease, with earlier clinical manifestations. As a consequence, the number of young children with type 1 diabetes requiring care has risen significantly along with an increased burden on the healthcare system as well as on the families of these young patients.

The rates of progression in diabetes incidence vary from country to country and with different age groups. In France, the incidence was accurately measured during 1988–1997 through the French Registry of Incidence of Diabetes, which documented an annual increase of 3.4% in patients before age 20, with the last known incidence rate being 9.6 per 100,000 population [3]. However, no data have been published since 1998 at either the national or regional level. Nevertheless, from a public-health perspective, there are two important questions:

- is the increasing trend persisting over time?
- is the rate of progression linear or accelerating over time?

To answer to these questions, we carried out a regional study in Aquitaine to assess the pattern of incidence of type 1 diabetes in children registered over a 17-year period (1988–2004).

2. Patients and methods

2.1. Patients

Type 1 diabetes was defined according to World Health Organization criteria [4] and the presence of a permanent need for insulin therapy. The date of the first insulin injection was taken as the date of inclusion into the study. Cases of neonatal diabetes were excluded from the present study because of the age at diagnosis: for inclusion, patients had to be aged greater than six months and less than 15 years at the time of diabetes diagnosis, and have a permanent residential address within the region of Aquitaine in France.

2.2. Registration of cases

From 1988 to 1997, new cases of type 1 diabetes were confirmed on registration into the French Registry of Incidence of Diabetes, according to methods previously described in detail [5]. This prospective registration met the inclusion criteria of the Eurodiab study, which used two direct and independent sources for identification of cases [6]. Various hospital units for adults and children as well as private hospitals and practitioners in private practice were selected as the primary sources of information. Data from the French national health insurance system (Social Security) was the secondary independent source of cases identification. The rate of confirmed cases was calculated using the "capture–recapture" method, and was greater than 95% over the study period. The Registry operated from January 1, 1988 and December 31, 1997. All qualifying cases of type 1 diabetes arising between these two dates were included in the study.

Registered cases were also collected from hospital-based prospective records from all paediatric centres in the Aquitaine area (Agen, Bayonne, Bergerac, Bordeaux, Dax, Libourne, Marmande, Mont de Marsan, Pau, Périgueux and Villeneuve-sur-Lot) to create a diabetes medical network, the Association de diabétologie infantile en Aquitaine (ADIA). Although the healthcare guidelines in Aquitaine recommend that children to be directed to paediatric centres at the onset of diabetes, diabetologists in this region have also been contacted to assess isolated cases unrecognized by paediatric centres.

2.3. Population base

The study population was made up of children aged less than 15 years in Aquitaine, representing approximately 5% of the French age-matched population. These numbers, provided by the Institut national de la statistique et des études économiques (INSEE), are also available for other age groups, for both genders and for each of the 17 years covered in the study.

2.4. Calculation of incidence rates

The numerators were made up of all cases identified by either of our case sources. Age was calculated for each individual using the fully attained age on the first day of insulin therapy. Incidence rates were calculated for the overall study population, for each age group (0–4 years, 5–9 years, 10–14 years) and for each gender. Standardized incidence rates were calculated based on a direct calculation, which assumed that the standard population was distributed in groups of equal size and defined by age and/or gender.

2.5. Statistical analysis

The trend in incidence rates was tested using the Poisson regression, where the standardized incidence rate is the dependent variable and the calendar year is the independent variable.

Table 1
Newly diagnosed cases of type 1 diabetes and the reference population (per year) presented according to age and gender, registered during 1988–2004 in Aquitaine.

Year	Age 0–4 years				Age 5–9 years				Age 10–14 years			
	Boys		Girls		Boys		Girls		Boys		Girls	
	n	Ref pop	*n*	Ref pop	*n*	Ref pop	*n*	Ref pop	*n*	Ref pop	*n*	Ref pop
1988	6	80,432	3	77,017	7	88,063	9	83,620	7	91,448	13	87,099
1989	4	81,015	3	77,398	5	88,294	6	83,962	13	88,261	12	84,258
1990	4	81,408	4	77,902	10	87,905	6	83,688	12	87,589	10	83,232
1991	5	81,498	4	77,997	5	86,751	7	82,534	12	89,380	8	84,636
1992	2	81,260	2	77,479	7	85,708	5	81,864	10	91,381	9	86,121
1993	3	80,764	3	76,997	6	85,005	9	81,361	13	92,356	13	86,917
1994	1	79,466	3	75,643	16	85,650	7	81,668	10	92,113	12	87,044
1995	4	78,533	5	74,484	10	85,975	10	82,010	18	91,535	13	86,643
1996	6	77,940	5	73,874	8	85,969	8	82,098	16	89,971	11	85,208
1997	5	77,625	1	73,928	6	85,770	9	81,593	16	88,725	10	84,446
1998	3	77,893	10	73,832	10	85,319	9	81,179	13	87,942	5	83,940
1999	5	79,080	7	74,885	7	84,332	10	80,088	11	88,801	12	84,444
2000	6	80,391	9	76,538	7	83,780	15	79,164	12	89,562	12	85,372
2001	3	82,506	12	78,506	15	83,485	4	78,878	14	90,391	10	86,030
2002	9	84,310	9	79,863	9	83,561	9	79,449	14	90,754	10	86,029
2003	7	86,065	9	81,446	18	84,120	19	79,367	14	90,804	13	86,308
2004	11	87,267	8	82,909	12	85,474	8	80,878	14	90,317	16	85,322
Total	84		97		158		150		219		189	

Ref pop: reference population.

For analysis by age, an analysis of covariance (Ancova) was performed to test whether the slopes could be considered equal. For analysis by gender, the alignment of the linear-regression lines fitted for each group was tested. Again, Ancova was used to test whether the slopes could be considered equal. All analyses were performed using Stata Statistical Software: Release 7 SE (Stata Corporation, College Station, TX, USA).

3. Results

A total of 897 patients (461 boys, 436 girls) were included in the study. Table 1 shows the number of type 1 diabetes cases included each year, according to age and gender. No significant difference was observed in the gender ratio between patients and the reference population. In the overall population, the age- and gender-adjusted incidence rate increased from 8.86 per 100,000 population per year (95% confidence interval [CI]: 6.27–11.45) in 1988 to 13.47 per 100,000 population per year (95% CI: 10.29–16.65) in 2004 (Table 2). Median age at the onset of diabetes in those from the first registration period (1988–1996) was significantly higher ($P = 0.01$) than that from the second registration period (1997–2004): 10.0 years (range: 6.6–12.5) versus 8.8 years (range: 5.5–11.7), respectively.

The annual increase in incidence for the overall population was 3.34% (95% CI: 3.33–3.34), an increase that remained statistically significant throughout the study period ($P < 0.001$). Also, the gender-adjusted incidence rate significantly increased in each of the three age groups, while the slopes of the regression lines were significantly different across the three age groups ($P < 0.001$). As shown in Fig. 1, the annual increase was the greatest among the youngest children (0–4 years: 7.59%; 5–9 years: 4.06%; 10–14 years: 1.28%).

Table 2
Annual age- and gender-adjusted incidence rates of type 1 diabetes in Aquitaine children aged greater than 15 years

Year	*n*	Reference population	Incidence per 100,000 per year	95% CI
1988	45	507,679	8.86	6.27–11.45
1989	43	503,188	8.54	5.99–11.10
1990	46	501,724	9.16	6.52–11.82
1991	41	502,796	8.15	5.66–10.65
1992	35	503,813	6.95	4.65–9.25
1993	47	503,400	9.34	6.67–12.01
1994	49	501,584	9.77	7.03–12.50
1995	60	499,180	12.00	8.98–15.06
1996	54	495,060	10.90	8.00–13.82
1997	47	492,087	9.55	6.82–12.28
1998	50	490,105	10.20	7.37–13.03
1999	52	491,630	10.58	7.70–13.45
2000	61	494,807	12.33	9.23–15.42
2001	58	499,796	11.60	8.62–14.59
2002	60	503,966	11.90	8.89–14.92
2003	80	508,110	15.74	12.29–19.19
2004	69	512,167	13.47	10.29–16.65
Total	897			

4. Discussion

Data from the ongoing registration in Aquitaine of newly diagnosed cases of type 1 diabetes showed a 52% increase in the incidence of the disease in children less than 15 years of age over the 17-year study period, corresponding to a constant annual increase of 3.3%. Moreover, this increase was especially pronounced among the youngest children: 7.6% in those aged 0–4 years.

Aquitaine is a geographically well-delineated area in the southwest of France where paediatric centres also participated

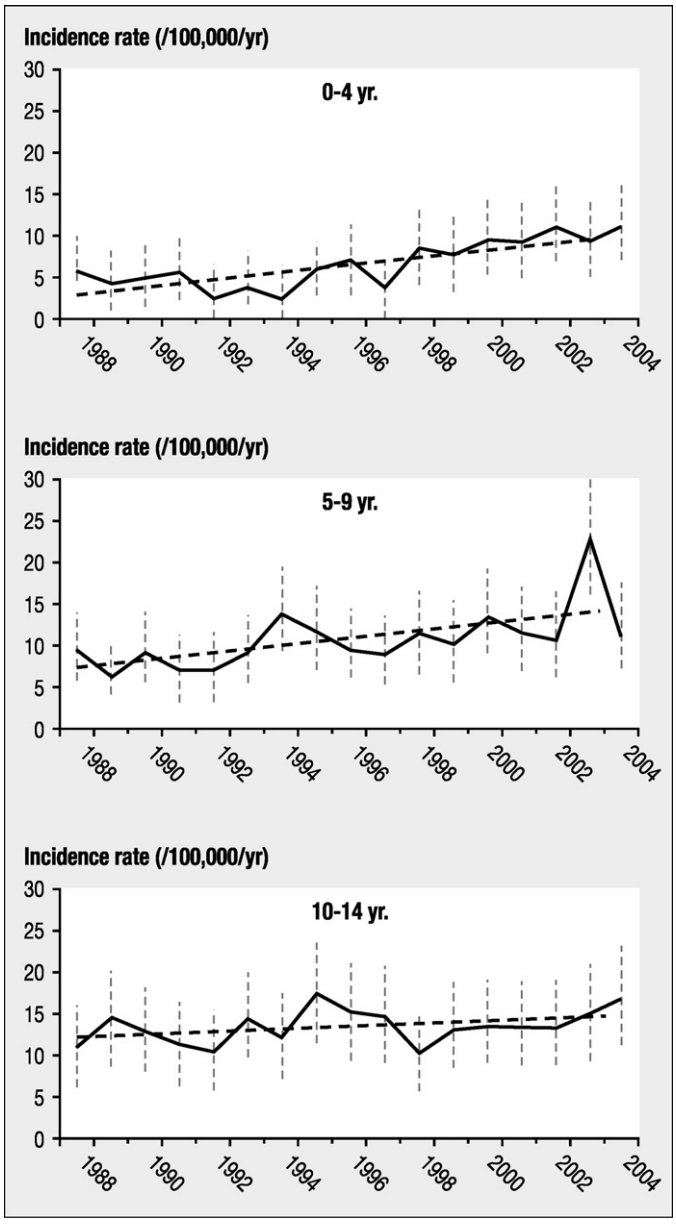

Fig. 1. Time course of incidence rates across age groups. These are gender-adjusted incidence rates (number of cases/100,000 population/year ± S.D.) of type 1 diabetes in children aged 0–4, 5–9 and 10–14 years in Aquitaine during 1988–2004. The dotted line represents the regression curve for each age group.

in the Eurodiab study in the 1990s and so, were accustomed to collaborating through a regional network. These facts allowed us to present updated incidence rates of type 1 diabetes in children aged greater than 15 years (approximately 5% of the French population) to cover the 17-year period of registration.

One limitation of our analysis is that it is based on two different sources over time: one is a population registry; the other is hospital-based records. However, the inclusion criteria for the two were identical. It may be argued that the latter source of registration is not as complete as a proper registry. However, results from the earlier years of the French Registry showed that more than 99% of children were hospitalized at the time of initiation of insulin therapy, irrespective of the age at onset [7]. As our study is restricted to type 1 diabetes – defined as insulin-dependent diabetes – very few cases are likely to have been missed in the second registration period. However, even if this was to be the case, the result would be a reduction in incidence rates. This would mean that the increase observed across our two study periods is an underestimation of the true incidence rate, although the overall conclusion would remain the same as only the rates during the second period (1998–2004) would be slightly lower than they should be. Nevertheless, the overall increase reported here is in the same order of magnitude as those described in the French Registry for France as well as for the whole of Europe [3,8]. Moreover, the latest data (for 2005), released by the French national healthcare insurance branch (*Assurance Maladie*) indicates a rate of 15.5 per 100,000-population aged greater than 15 years in the entire country [9].

Until the late 1980s, the incidence of diabetes in children in France was considered by one review to be among the lowest in Europe [10]. With an incidence rate of 13.5/100,000 in 2004 – up from 8.9/100,000 population in 1988 – Aquitaine represented an area similar to Belgium or Spain, with a rate still far lower than in the "top-ranking" regions of Europe [11]. This upward trend has been constant over 17 years and the progression is linear, increasing at a rate of 3.3% each year, which means that the incidence of type 1 diabetes in children may be expected to double in 30 years.

Furthermore, the most recent data from Finland shows that, not only has the incidence rate increased over the last 25 years at an annual rate of 3.0%, but there is also a significant non-linear trend in relation to time. In the Finnish cases, the increase was also more pronounced in children aged 0–4 years [12]. Coming from the country with the persistently highest incidence rates in the world, this observation highlights the importance of monitoring the incidence of type 1 diabetes to provide actual and updated figures from the clinical and public health points of view.

The large increase of incidence among the youngest children together with the modest increase in those, who were older is consistent with the younger age of diabetes onset seen at the end of the 17 years of registration, and has several implications. Firstly, diabetes care in young children – and especially in toddlers – is highly specific and demanding both on the patients' families, and on medical and nursing teams. Greater glycaemic instability, a higher risk of severe hypoglycaemia with seizures and interference from febrile illnesses, which are particularly frequent at this age, are only some of the critical issues. Secondly, whatever the new preventative interventional strategy, when tested in trials, it will have to be safe enough to be given to young children if its effectiveness in controlling the disease is the objective.

Faced with diabetes in young children, the paediatric centres in Aquitaine have had to adapt their healthcare provision over the past 17 years. In future, the growing incidence rate coupled with a younger age at diagnosis will further increase the burden on paediatric centres and, consequently, lead to a more time- and staff-consuming situation that will need to be taken into consideration by the healthcare system in general.

Acknowledgements

The authors are grateful for the contributions of all members of the ADIA and, in particular, wish to thank M. Carre (Bayonne), J.M. Cazauran (Périgueux), J. Chevrel (Dax), B. Guerin (Pau), M. Joussein (Agen), J. Peyraud (Libourne) and M.L. Pignol (Mont de Marsan).

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