

An eBook on Diabetes

Chapter 5

Time Trend and Onset Characteristics of IDDM Cases in Subjects Aged 0-29 Years in the Province of Trento. A Comparison between Italians and Foreigners

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Abstract

Objectives

The study reports the time trend and onset characteristics of type 1 Diabetes (IDDM) cases amongst subjects aged 0-29 years in the resident population of the province of Trento for the period 1.1.1998-31.12.2017, comparing Italians and foreign nationals.

Study Design

The source of the cases is represented by the provincial registry of IDDM which is part of the national RIDI (Italian register of insulin-dependent diabetes) network. The primary information source of the registry is the standard RIDI sheet, integrated by two secondary information flows: data regarding co-payment exemption for diabetes and hospital discharge records. The date of incidence is defined, for each case, by the date of the first insulin administration. We calculated the total number of cases registered in the study period, the number of new cases and the proportion of foreigners

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per year. The trend of the incidence rate between Italians and foreigners is represented as a three-year moving average. The clinical characteristics at the onset of IDDM among Italians and foreigners are analyzed on the basis of the frequency of ketoacidosis (DKA). Factors associated with onset with DKA are then assessed through a multiple analysis.

Results

Between 1998 and 2017, the Province of Trento RIDI Registry recorded 421 cases of IDDM amongst residents aged 0-29 years, 21 cases per year. Males were 53% and the prevalent age range is 0-14 years, which constitutes 67.4% of cases. 52 cases (12.4%) are to be considered foreign nationals. The proportion of cases of foreign nationality increased over time, from 5.9% in 1998 to 34.9% in 2017, with a statistically significant trend ($p < 0.01$). The average age at disease diagnosis over the study period is 10.9 years for foreign nationals and 12.0 years for Italians. The incidence rate is higher amongst foreign nationals than Italians both across the entire 0-29 years caseload and within the individual pediatric age classes. Ketoacidosis is present at clinical onset in 39.2% of cases: 55.7% amongst foreign nationals and 36.9% amongst Italians. Foreign nationality represents an independent risk factor for ketoacidosis at onset of IDDM.

Conclusions

In the study period there is an increasing trend of IDDM cases aged 0-29 years in the foreign population, associated with the increase of the foreign population, observed in the province of Trento. Being a foreigner represents an independent risk factor for the clinical onset of IDDM in ketoacidosis. Health services will need to implement specific actions to address this phenomenon.

Keywords: Type 1 Diabetes, Childhood and young adults, Temporal trend, Ketoacidosis, Citizenship.

1. Introduction

Diabetes is one of the most frequently-observed chronic diseases amongst the pediatric population, in which the most common form is type 1 diabetes (IDDM) followed by genetic diabetes and type 2 diabetes [1]. Systematic registration of new cases of the disease is important for being able to describe its distribution and trends, investigate the risk factors and study the healthcare response and the corresponding costs, as indicated by the Italian National Diabetic Disease Plan [2]. Given the current trend of the disease among children and young adults, the availability of registration systems in several countries has made it possible to specifically

study the trends of IDDM among immigrants [3-11]. These studies also make it possible to identify the effect of environmental changes on the incidence and characteristics of the disease, also in consideration of the fact that over the past two decades the number of immigrants entering various European countries, including Italy, has increased approximately 3-4-fold, especially amongst the younger age groups. This trend has also been observed in the province of Trento, where between 1998 and 2017 the number of resident foreign nationals rose 4.4-fold (from 10,665 in 1998 to 46,929 in 2017). In 1998, Trento Provincial Health Authority (APSS) joined the RIDI (Italian Insulin-dependent Diabetes Register) network, which was established to acquire epidemiological data on new cases of IDDM in the 0-29-year age range. The study reports the time trend and onset characteristics of IDDM cases amongst subjects aged 0-29 years in the resident population of the province of Trento (540,000 inhabitants at 31.12.2017), for the period 1.1.1998-31.12.2017, making a distinction between Italian and foreign nationals.

2. Materials and Methods

The provincial RIDI Registry is based on a primary information flow, namely the standard RIDI sheet that, until 2013, was submitted by the Diabetes Centers to the Provincial Health Authority's Epidemiology Service as a paper form. Since 2014, the annual data has been transferred electronically. The completeness of the primary information source is verified using two secondary information flows, namely data regarding co-payment exemption for Diabetes (Code 013) and hospital discharge records. For those cases identified solely by means of these latter two flows, the competent Diabetes Centre subsequently has to fill out and submit the RIDI sheet. The Epidemiology Service retrieves any missing data for the specified variables, such as the biochemical status at onset, by accessing the Hospital Information System (HIS), a repository containing all the relevant clinical data for users who come into contact with the Provincial healthcare service. The date of incidence is defined, for each case, by the date of the first insulin administration. We calculated the total number of cases registered in the study period, the number of new cases and the proportion of foreigners per year. The temporal trend for resident cases is reported in relation to nationality (Italians vs foreign nationals), considering gender, age range and class and age-specific rates. The latter are provided as exact annual figures and averages for the period, in order to minimize annual variability, considering the relative consistency of the population. Nationality-based data is provided regarding the clinical characteristics of the disease at onset for Italians and foreign nationals, using the proportion of cases with ketoacidosis (DKA) at onset as the representative criterion. The criteria used to define DKA are those proposed by the SIEDP (Italian Pediatric Endocrinology and Diabetology Society), namely DKA is present when $\text{pH} < 7.30$ and/or Bicarbonate < 15 mEq. Trend significance was analyzed using the Cochran-Armitage criterion and the significance of the differences between the proportions was analyzed using the chi squared

test or Fisher's exact test. Incidence data are provided with the 95% confidence intervals. The factors associated with the onset of DKA were studied using multiple logistic regression analysis, in which the explanatory variables considered were gender, age range, nationality, country of birth, territorial area of residence (rural vs urban) and altitude of residence (low-lying/hilly/mountainous area). The statistical analyses were performed using the Epi-Info package.

3. Results

Between 1998 and 2017, the Province of Trento RIDI Registry recorded 421 cases of IDDM amongst residents aged 0 - 29 years, 21 cases per year. Males prevailed over females (53% vs 47%), especially in the older age classes. The prevalent age range was 0-14 years, which represented 67.4% of the cases observed over the study period. The trend oscillated greatly until 2011, the year in which the lowest number (14 cases) was recorded; from 2012 onwards, there was an increase in the figure, followed by an apparent stabilization in the number of new cases recorded each year (**Figure 1**). 84% of cases were born in Trento province, 11.7% in other Italian regions and 4.3% were born abroad. In 19.0% of cases at least one parent was born abroad and one in three foreign parents born abroad comes from a country with high migratory pressure. According to the nationality-attribution criteria used in Italy, 52 cases (12.4%) are to be considered foreign nationals. Of these, 41 were born in Italy, 6 in Eastern European countries, 3 in Africa, 1 in Asia and 1 in Central/Western Europe. The proportion of cases of foreign nationality increased over time, from 5.9% in 1998 to 34.9% in 2017, with a statistically significant trend ($p < 0.01$) (**Figure 2**). Of the total number of foreign cases, the proportion of subjects in the 0-14 years age range is slightly higher than amongst Italian nationals (69.2 vs. 67.2%), a difference that is greater amongst females (80.9 vs. 70.6%) (**Table 1**). The average age at disease diagnosis over the study period is 10.9 years for foreign nationals and 12.0 years for Italians. The average age at diagnosis trend is also characterized, as a three-year moving average, by an increase in foreign nationals from 2006 and a decrease in Italians. The average age, over the last three years considered, would appear to be similar for the two groups (**Figure 3**). The incidence rate of IDDM is higher amongst foreign nationals than Italians both across the entire 0-29 years caseload and within the individual pediatric age classes. More specifically, amongst Italian nationals the average annual incidence rate in the 0-29 years age range is 13/100,000/year (95% CI: 11.7-14.2) and increased from 10.2/100,000 (1998) to 11.0/100,000 (2017); amongst foreign nationals it is 16.6/100,000/year (95% CI: 12.3-20.9) and rose from 13.3/100,000 to 43.1/100,000. Amongst Italian nationals the average annual incidence rate in the 0-14 years age range is 17.5/100,000/year (95% CI: 17.3 - 17.6) and decreased from 11.7/100,000 to 11.5/100,000; amongst foreign nationals it is 24.9/100,000/year (95% CI: 17.1-32.7) and increased from 16.6/100,000 to 65.0/100,000. Amongst Italian nationals the average annual incidence rate in the 0-4 years age range is 14.9/100,000/year (95%

CI: 11.6-18.2) and increased from 8.45/100,000 to 19.5/100,000; amongst foreign nationals it is 18.4/100,000/year (95% CI: 8.1-28.7) and increased from 0 to 25.8/100,000. Amongst Italian nationals the average annual incidence rate in the 5-9 years age range is 17.2/100,000/year (95% CI: 13.7-20.7) and decreased from 8.7/100,000 to 8.3/100,000; amongst foreign nationals it is 30.9/100,000/year (95% CI: 15.1-46.7) and increased from 36/100,000 to 70.2/100,000. Amongst Italian nationals the incidence rate for the 10-14 years age range is 20.5/100,000/year (95% CI: 16.6-24.4) and decreased from 18.1/100,000 to 7.9/100,000; amongst foreign nationals it is 28.0/100,000/year (95% CI: 12.4-43.6) and increased from 0 to 82.4/100,000. DKA is present at clinical onset in 39.2% of cases (165 subjects), a situation that is slightly more common in females than in males (41.4% vs 37.2%). The prevalence of DKA over the entire study period is 55.7% amongst foreign nationals and 36.9% amongst Italians; this difference is statistically significant ($p < 0.05$). The higher prevalence of DKA amongst foreign nationals than amongst Italians is present in almost all age classes, with a higher value, in the 0-4 years and 15-19 years age ranges (**Table 2**). DKA trend amongst Italians and foreign nationals, considered as a three-year moving average in order to minimize extreme annual variations, reveals values that are almost constantly higher for foreign nationals and in Italians takes on decreasing values from 2009 (**Figure 4**). When other conditions are equal, foreign nationality represents an independent risk factor for ketoacidosis at onset of insulin-dependent diabetes mellitus in children and young adults (**Table 3**).

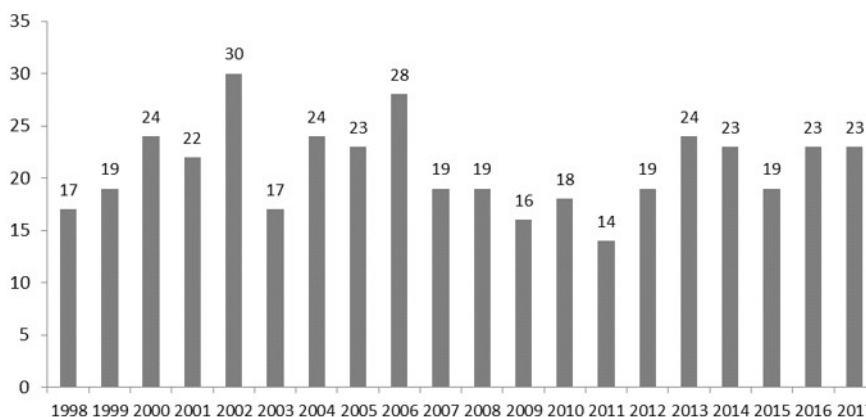


Figure.1: Province of Trento. IDDM cases amongst the resident population aged 0-29 years. Males and Females. Per single year. Period 1998-2017.

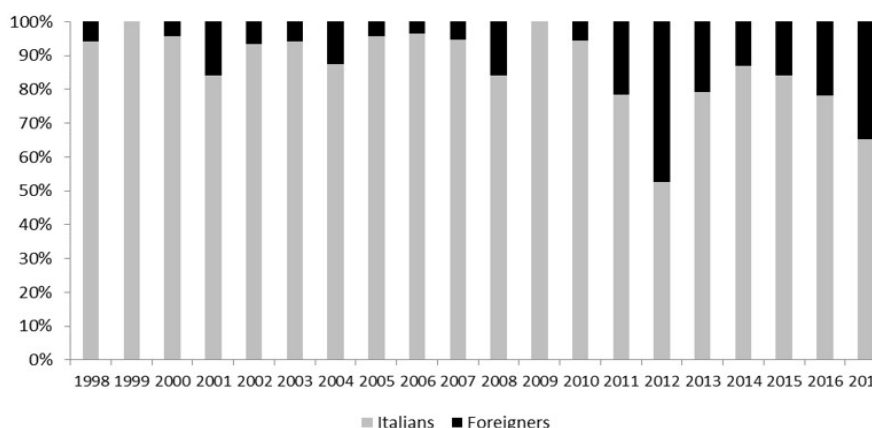


Figure 2: Province of Trento. Proportion of subjects of foreign nationality out of total cases of IDDM recorded in the resident population aged 0-29. Per single year. Period 1998-2017.

Table 1: Province of Trento. Distribution by gender and age class of cases of IDDM in the resident population. Italian vs. Foreign nationals. Period 1998-2017.

Nationality	Males					Females					Total M	Total F
	0-4	5-9	10-14	15-19	20-29	0-4	5-9	10-14	15-19	20-29		
Italian	31	31	61	19	50	38	52	35	19	33	192	177
Foreign	8	7	4	4	8	3	7	7	2	2	31	21
Total	39	38	65	23	58	41	59	42	21	35	223	198

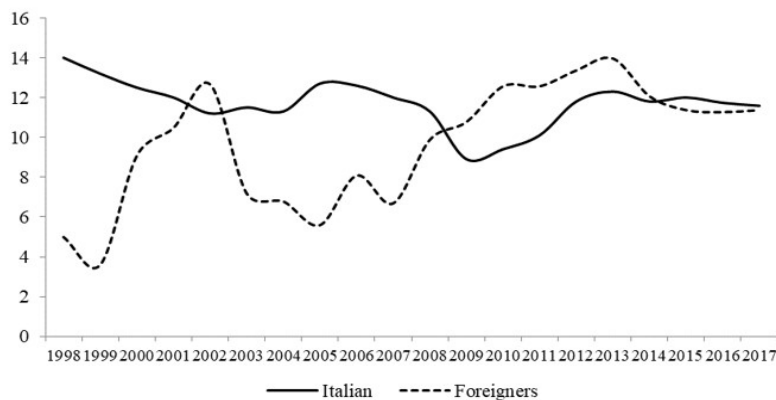


Figure 3: Province of Trento. Moving average of the mean age at onset of IDDM, Italian vs foreign nationals. Period: 1998-2017.

Table 2: Province of Trento. Frequency of DKA at onset of IDDM by age class and nationality. Period 1998-2017.

Nationality	Age class				
	0-4	5-9	10-14	15-19	20-29
Italians	39.7%	30.9%	31.6%	47.1%	32.4%
Foreign nationals	70.0%	50.0%	27.3%	80.0%	55.6%

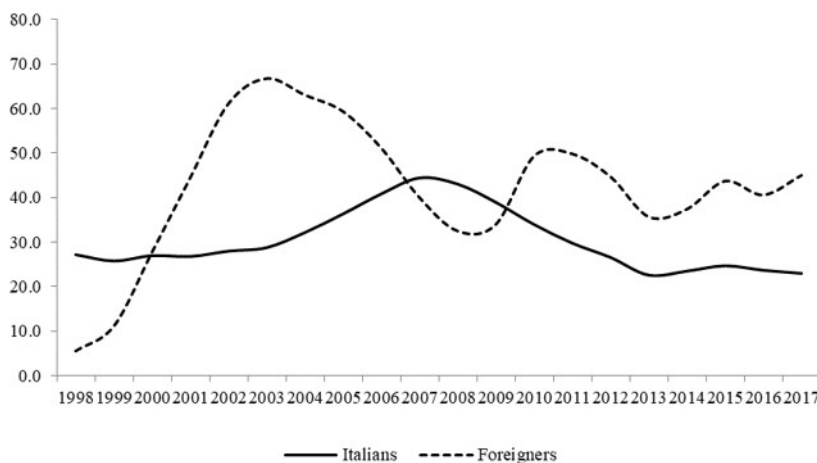


Figure 4: Province of Trento. DKA at IDDM onset. Three-year moving average of the proportion of cases. Italian vs. foreign nationals. Per single year. Period 1998-2017.

Table 3: Factors associated with the risk of DKA at IDDM onset. Adjusted Odds Ratio and 95%CI.

Parameters	Odds Ratio	95% CI		p-value
Gender: Females vs males	1.16	0.77	1.76	0.46
0-4 vs. 5-29 years age classes	1.43	0.85	2.41	0.16
Nationality: Foreign nationals vs Italians	2.21	1.14	4.27	0.01
Born abroad vs born in Italy	0.77	0.22	2.66	0.69
Territorial area: rural vs urban	0.68	0.27	1.05	0.20
Altitude: Hilly vs low-lying area	0.66	0.38	1.14	0.13
Altitude: Mountainous vs low-lying area	0.75	0.46	1.22	0.25

4. Conclusions

The burden of subjects of foreign nationality with IDDM aged 0-29 years in Trento province is rising, as reported in other areas of Italy [4,7,11]. This increased burden is expressed both by the increase in the proportion of cases included in the local RIDI registry, which rose from 5.9% in 1998 to 34.7% in 2017 and by the increase in the incidence rate, which in 2017, across the entire 0-29 years caseload, is 4 times greater than amongst Italian nationals. The difference between foreign nationals and Italians is even greater in the 5-9 years and 10-14 years age classes. The increasing trend of IDDM in foreign patients is associated with the increase in the foreign population, in the corresponding age classes, observed in the province of Trento, in the same way and perhaps to an even greater extent than in other regions of Italy over the study period.

Approximately 80% of foreign cases present in the local RIDI registry are recorded as having been born in Italy; in 4 out of 10 cases the parents are of African origin and in 3 out of 10 cases they are of Eastern European origin. All cases of foreigners whose parents come from North African countries were born in Italy. This finding appears to be consistent with other Italian studies [4,11]. The study also confirmed that on average foreign cases are younger than Italian cases. This may suggest the influence of environmental factors during the early years of life, which could include viral infections whose spread may be favored by the living and/or nutritional conditions of this more vulnerable category of the population. The body's diabetogenic response could be immune-mediated, due to a different genetic susceptibility and with a modulation that differs with age [12-16]. It should also be taken into account that in the African countries of origin, the available data shows that the incidence of IDDM amongst the pediatric/juvenile population is far lower than in European countries [17,18] and that a steep increase in incidence has been observed in recent years in Eastern European countries [19-21]. Lifestyle changes amongst resident immigrants could also explain the different increase in incidence compared to the parents' countries of origin [22]. The more rapid onset of the disease, combined with the probable greater difficulty in recognizing the symptoms, could explain why DKA at onset is more common amongst foreign nationals than amongst Italians [4,23,24].

Nevertheless, the similar distribution of cases of DKA according to age class between Italians and foreign nationals and the lack of variation in relation to the area of residence of the cases, expressed as rural vs urban area and level of altitude, would suggest a certain homogeneity in the care provided by the province of Trento healthcare services. The increasing burden and the greater severity of clinical onset in any case require an informative and educational approach that takes into account the ethnic aspects of the disease, also bearing in mind that compliance with the prescribed therapy tends to be poorer amongst foreign nationals than amongst Italians [25-28].

5. References

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