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Research paper

Seasonal variation of type 1 diabetes mellitus diagnosis in Greek children

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ABSTRACT

OBJECTIVE: The aim of the study was to investigate the seasonal variation of type 1 diabetes mellitus (T1DM) diagnosis in Greek children. DESIGN: The study group consisted of 1148 patients (604 males and 544 females) who were diagnosed with T1DM during the period 1978-2008. The mean age at diagnosis was 8.32±5.01 years. The date of birth and the date at diagnosis were recorded from the patients' files. RESULTS: Significantly more children were diagnosed with T1DM during the cold months as opposed to the warm months (p=0.001), with no differences between boys and girls. When children were categorized into the age groups ≤3 and >3 years old the seasonal variation pattern was different in younger ages suggesting that environmental factors which possibly interfere with T1DM diagnosis may have a different effect in those of younger than older age. With regard to date of birth, significantly more children with diabetes were born during the Spring-Summer than in Autumn-Winter (p=0.004). CONCLUSIONS: The results of the study support the concept of seasonality in T1DM diagnosis, implying a possible relationship between clinical expression of T1DM and various climatic factors. Seasonal variation at diagnosis appears to be different in younger compared to older children.

Key words: Diabetes mellitus type 1, Seasonal variation, Viral infections

INTRODUCTION

The current concept of the etiology and pathogenesis of type 1 diabetes mellitus (T1DM) includes environmental factors, which in a genetically susceptible individual, trigger an autoimmune process in the pancreas leading to damage of beta cells.[1] Among these environmental factors, the most extensively studied is the exposure to enteroviral infections.[2] Since these infections demonstrate seasonal fluctuations, many studies have tested the hypothesis that the diagnosis of diabetes may also display seasonality patterns.

The first report of seasonal variation in the new cases of T1DM was presented by Franklin Adams in the 1920s.[3] Since then, there have been a number of studies demonstrating seasonality in the time of clinical presentation of T1DM, although a consistent and integrated picture on the actual seasonality of

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the disease has not been established.[4-15] It has been suggested that there is also a relationship between factors such as infections and vitamin D levels, and the seasonality of T1DM.[16-18] A recent meta-analysis of the data on seasonal variation in diabetes in 53 countries has suggested that seasonality in the diagnosis of T1DM is indeed a real phenomenon and that this seasonality pattern appears to be related to the geographical position, at least as far as the northern/southern hemisphere is concerned.[19] However, data on many regions of the world are still lacking.

This study was conducted in order to investigate the possibility of seasonality in the initial presentation of T1DM in a Greek cohort.

SUBJECTS AND METHODS

Subjects

This is a retrospective study which includes data on the initial presentation of 1148 children (604 males and 544 females) with T1DM attending the Diabetes Center of the Department of Pediatrics, Faculty of Nursing of the University of Athens, at the P. & A. Kyriakou Children's Hospital. The study was approved by the Hospital Review Board. The patients originated from both urban and rural Greek regions. The mean age of the patients at diagnosis of T1DM was 8.32±5.01 years (range 0.1 to 16.4). All children included in the study had T1DM.

Measures

The date of birth and the date of T1DM clinical diagnosis were obtained from the patient's files.

Definitions

The subjects were divided into groups according to the month of birth or diagnosis as follows: November, December, January and February were defined as cold months, September, October, March and April as moderate, and May, June, July and August as warm months. Subjects were also grouped according to the season of birth or diagnosis as follows: Autumn-Winter (September to February) and Spring-Summer (March to August). In addition, subjects were also divided into two groups according to age at diagnosis: aged ≤3 years and >3 years. This age cut-off point was selected on the basis of current data suggesting an increase in the prevalence of diabetes in the lower age groups.[6,20,21]

Statistical analysis

Data are presented as means ± 1 standard deviation or as percentages. The Pearson chi square test was used to assess statistical significance in all two-way and goodness of fit tables. Statistical significance was set at $p<0.05$. All analyses were performed using the SPSS 11.0 package.

RESULTS

Significantly more children were diagnosed with T1DM during the cold months in comparison to the warm months, with intermediate values during the moderate months (cold vs. warm $p=0.001$, cold vs. moderate $p=0.0192$, moderate vs. warm $p=0.09$), Figure 1. Thus, the number of children diagnosed with T1DM was higher during November, December, January and February ($p=0.001$): 55.79% of boys were diagnosed during Autumn-Winter and 44.21% were diagnosed in Spring- Summer ($p=0.001$). The corresponding values for girls were 56.25 and 43.75% ($p=0.001$). No significant differences were observed between boys and girls ($p=0.376$) with regard to the seasonal variation of clinical presentation of T1DM.

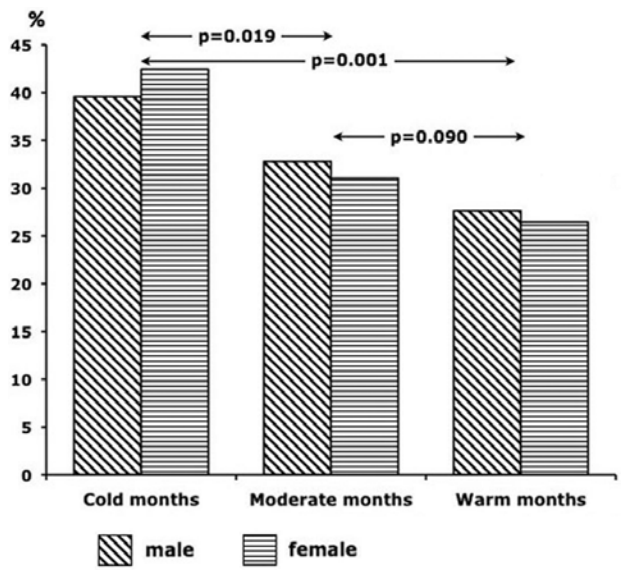

Figure 1. Percentage of children diagnosed with Type 1 Diabetes by gender at different environmental temperatures. No gender differences.

No differences were found in the monthly variation of the date of birth, neither in the total patient population (p=0.164) nor separately for each gender (p=0.855). However, in the total group more children with T1DM were born in Spring-Summer than in Autumn-Winter months (52.83% vs. 47.17%, respectively, p=0.004) (Figure 2). A statistically significant higher proportion of boys were born during the Spring-Summer as opposed to the Autumn-Winter months (53.31 vs. 46.69%, respectively, p=0.02). The difference observed in girls was not significant between those who were born during the Spring-Summer compared to those born during the Autumn-Winter months (52.21 vs. 47.79%, respectively, p=0.08).

When data were analyzed according to age at diagnosis (less than 3 and older than 3 years), it was found that the two age groups have different patterns of seasonal variation (Figure 3), p=0.004. Specifically, in the ≤3 years age group, more children were diagnosed with T1DM during the warm months compared to the cold months (p=0.026), while in the >3 years age group more children were diagnosed in the cold months compared to the warm months (p=0.007). No seasonality in the dates of birth was observed after grouping the children into the two age groups (p=0.37).

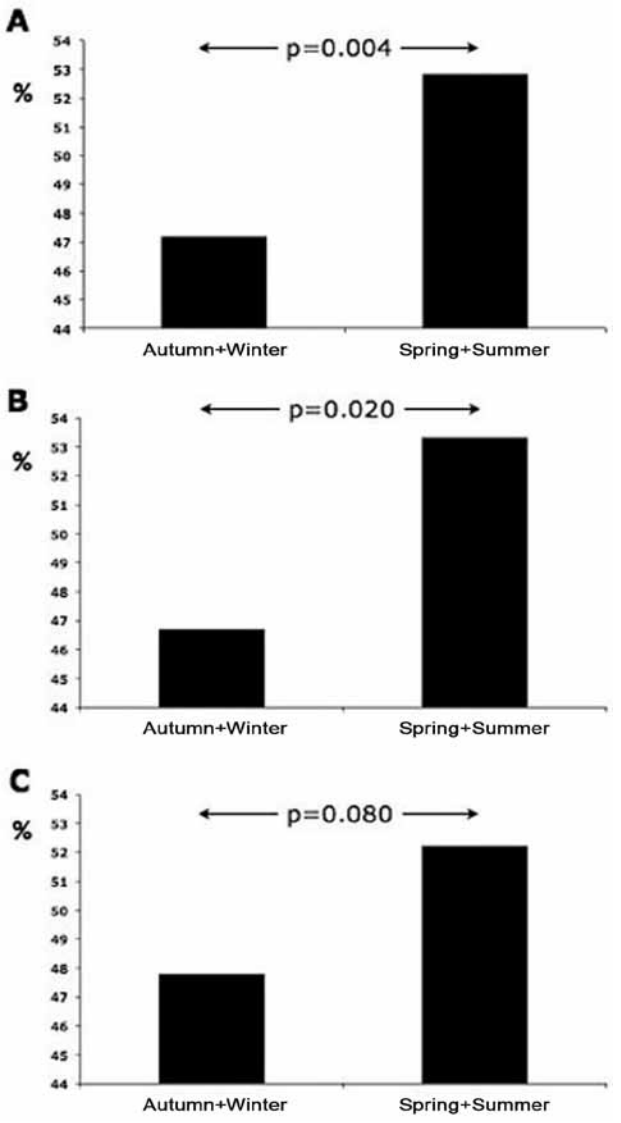

Figure 2. Percentage of children diagnosed with type 1 diabetes according to the season of birth and gender.
A: total population, B: boys, C: girls.

DISCUSSION

A significant seasonality in the incidence of T1DM diagnosis was found in both genders with peak values occurring during the cold months. The findings of this study are in agreement with other studies[4,7,9,11-14,19] supporting the seasonality in T1DM diagnosis. Rosenbauer et al[22] found a greater number of children diagnosed with T1DM during the Summer-Autumn period as opposed to the Winter-Spring period. Gray et al[4] and Scott et al,[12] on the other hand, have found seasonality in diagnosis only in boys. The increased

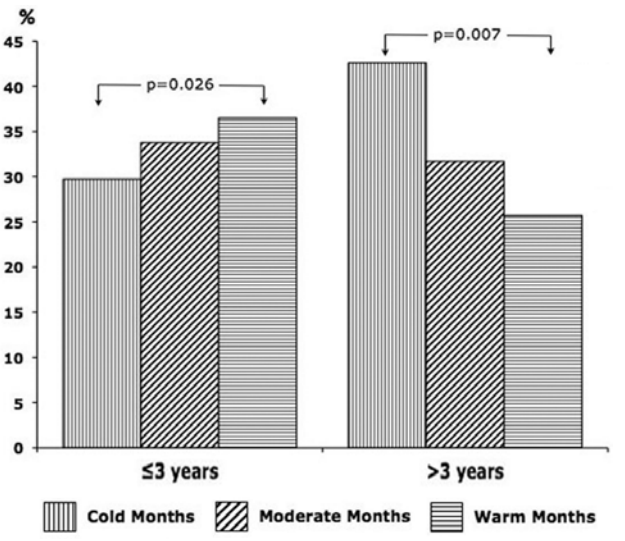

Figure 3. Percentage of children diagnosed with type 1 diabetes in the different age groups (≤3 vs. >3 years old).

incidence of T1DM diagnosis during Autumn and Winter months could support the hypothesis that infections may act as precipitating factors in the clinical manifestation of the disease, possibly accelerating an autoimmune process that may have been initiated months or years before.[16,23]

Moreover, the present study showed that the pattern of seasonality is different in children less than 3 years old, with the peak incidence occurring during the warm months, a phenomenon which is not easy to explain. Even if one hypothesizes that in the subjects less than 3 years old infections during foetal life play a role in the development of T1DM, the difference in seasonality in this group remains unexplained.

The date of birth also showed seasonal variation. Contrary to our findings, McKinney maintained that there is no relationship between T1DM diagnosis and the date of birth.[8]

In conclusion, seasonality of T1DM diagnosis is also encountered in the Greek population, with different patterns observed in younger compared to older children. This is the first study exploring the seasonality of T1DM in Greece. Nevertheless, it should be stated that this is an observational study on the seasonality of T1DM diagnosis from which no conclusions can be drawn regarding the pathophysiology of diabetes. A major limitation of our study is the time period of the collection of the data (30 years). Over such a time period, changes in unidentified environmental factors could have confounded our results. Another limitation of the present study is that our sample is not a random one for the total population in Greece and that we were not able to collect data on the geographical origin of each participant, a factor that could also have influenced our results. A previous work from Greece, however, showed that the incidence of T1DM is higher in big cities than in rural areas.[24] Prospective studies with larger numbers of T1DM patients are needed to confirm the issue of seasonality of T1DM diagnosis, thus possibly offering data on the etiology and epidemiology of this disease. A comparison with viral epidemiology data during the same period could likely yield useful results.

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