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Research

The Incidence and Demographical Distribution of Type 1 Diabetes Mellitus in Children Aged 16 or Younger Between 2000 and 2016 in Cyprus

Mousa U et al. Type 1 diabetes in North Cyprus

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What is already known on this topic?

The incidence of Type 1 diabetes has been reported in various countries. We do not know the incidence in our Country.

What does this study add?

This study is the first to report the incidence of pediatric age type 1 diabetes in our country.

Abstract

Objective: Type 1 diabetes (T1D) is a disease characterized by severe insulin deficiency. In 2008 our group studied the prevalence of diabetes in adults between 20-80 years of age. Data regarding subjects in the pediatric population is lacking. The objective of this study was to reach the incidence of type 1 diabetes among permanent inhabitants aged 16 or younger between 2001-2016 in Northern Cyprus.

Methods: This study was a retrospective analysis. The patients were mainly evaluated and recorded at B. Nalbantoglu Hospital in Nicosia. We also reviewed the data of Famagusta Government Hospital, Kyrenia Government Hospital, Near East University Hospital and the Cyprus Turkish Diabetes Association.

Results: A total of 107 subjects were diagnosed as T1D between 2001 and 2016 in this age group. Forty-nine (45.7%) were girls and 58 (54.3%) were boys. 38.7% were residing in Nicosia, 30.2% Famagusta, 12.3% Kyrenia, 9.4% Guzelyurt and 7.5% Iskele. The proportion of newly diagnosed T1D was highest among children aged 9-12 years (35.5%) followed by children aged 5-8 years (32.7%). Newly diagnosed T1D were most frequently presented in April and March. The overall mean incidence rate was 11.1/100000 between 2001 and 2016. The incidence rates were similar and comparable among the years.

Conclusion: This study is the first to analyze the incidence of T1D in Northern Cyprus. Compared to other countries the incidence rate is intermediate. Our findings are similar to the incidence rates of T1D in South Cyprus and Turkey.

Keywords: Type 1 diabetes, incidence rate, North Cyprus

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Introduction

Type 1 diabetes (T1D) arises from the autoimmune destruction of pancreatic β -cells leading to a life-long dependence on exogenous insulin (1). The disease is most commonly presented in children and adolescents (2). It is also the most frequently encountered chronic disease of childhood (3).

The incidence and prevalence of this disorder are not uniform worldwide. A large variability has been reported among different populations. Seasonal variations have also been reported. The highest incidence is observed in Scandinavian countries whereas China and countries close to the equator have lower incidences (4-6).

Cyprus is an island located in the Mediterranean region. A study published in 2012 reported the incidence of type 1 diabetes in South Cyprus. The authors reported that the overall mean incidence rate was 12.46/100000 between 1990 and 2009. In the first study decade, the mean incidence rate was 10.8/100000. However, in the second study decade, the mean incidence rate was 14.4/100000. Thus, the authors concluded that the incidence of T1D was rising in Cyprus (6).

Sardinia is a Mediterranean island which has a higher incidence than expected from the geographical region. The incidence rate was reported as 38.8/100000 between 1989 and 1999 (5).

According to a diabetes survey which our group performed in 2008, the prevalence of diabetes between 20-80 years was 11% and prediabetes 18% in Northern Cyprus. Studies regarding the pediatric population are lacking (7).

In this study, we aimed to calculate the incidence rates of T1D in Northern Cyprus in subjects 16 years of age or younger between 2001 and 2016.

Subjects and Methods

The study was approved by the B. Nalbantoglu Hospital Ethical committee with research number. 026/19. The study was retrospective and did not involve interventions, thus we did not obtain informed consent from the parents.

North Cyprus is divided into 5 main districts. These are Nicosia, Kyrenia, Famagusta, Iskele, and Guzelyurt. According to the population survey which took place in 2011, a total of 59,315 permanent inhabitants are present between 0-16 years of age. The distribution of this population among districts is seen in Table 1 (8).

B. Nalbantoglu Hospital, which is located in Nicosia, is the only government hospital which has an Endocrinology Clinic. Thus, all pediatric patients with hyperglycemia are transferred to this department. While collecting the data, we used records from this hospital together with records from Girne Government Hospital, Famagusta Government Hospital, Cengiz Topel Government Hospital, and Near East University Hospital. Subjects are advised to have records in the Cyprus Turkish Diabetes Association which is a Non-Governmental Organization (NGO). We also used their data in order to confirm ours.

T1D was diagnosed according to International Society for Pediatric and Adolescent diabetes (ISPAD) 2018 clinical practice consensus guidelines (9).

Subjects eligible for the study were I) Subjects were Turkish Cypriots and permanent inhabitants in North Cyprus, II) Fasting blood glucose ≥ 126 mg/dl, low c peptide levels and at least one positive antibody (insulin antibody, islet antibody, glutamic acid decarboxylase antibody), III) Subjects were 16 years of age or younger, IV) Type 2 Diabetes, Monogenic diabetes, neonatal diabetes and other types of secondary diabetes were excluded.

We recorded the gender of the subject, the age of the subject at diagnosis, the year and month of diagnosis and the district that the subject was residing.

Statistical Analysis

We used the Statistical Package for Social Sciences (SPSS) version 17 for Windows in analyzing and interpreting the data. The incidence was calculated by using the number of cases reported each year by age group (0-4, 5-8, 9-12, 13-16) and sex (male or female). The incidence rates were calculated per 100000 years. Comparison of proportions and incidence rates were performed via the χ^2 test. A p-value <0.05 was considered statistically significant.

Results

According to our records, we had identified a total of 107 new cases of T1D between 2001 and 2016 in children and adolescents younger than 16. Of these 49 (45.7%) were girls and 58 (54.3%) were boys. The Male/Female ratio was 1.18:1. The median age of diagnosis was 9. The median age of diagnosis was the same in both sexes (i.e. the median age of diagnosis was 9 for girls and 9 for boys). According to the population survey in 2011, the total population of subjects aged 16 or younger was 59315. Out of these 30561 were boys and 28754 were girls. The mean annual incidence rates for boys was 11.86/100000 and for girls 10.65/100000.

The proportion of newly diagnosed T1D was highest among children aged 9-12 years (35.5%) followed by children aged 5-8 years (32.7%). The highest incidence rate was in children aged between 9-12 years as 17.6/100000. The lowest incidence rate was in children younger than or equal to 4 years as 5.75/100000. Proportions and incidence rates according to age groups are seen in Table 2.

The number of cases per year is seen in Figure 1. The overall mean incidence rate was calculated as 11.1/100000 between 2001 and 2016. Between 2001-2005 the mean incidence rate was 11.2/100000; between 2006-2010: 11.4/100000; between 2011-2016: 10.8/100000. The mean incidence rates were statistically similar among the year groups ($p>0.05$).

The highest proportion of T1D was in Nicosia. However, the highest incidence rate was observed in Famagusta as 14.2/100000. The lowest incidence rate was observed in Kyrenia as 5.8/100000. The incidence rates of T1D in Kyrenia was significantly lower than the other districts ($p<0.05$). The incidence rate in Famagusta was similar to that of Nicosia ($p>0.05$), and higher than that of the other districts ($p<0.05$) (Table 1)

Newly diagnosed T1D were most frequently presented in April and March (14.3%, 13.2% respectively). The monthly distribution according to time of T1D diagnosis is seen in Figure 2.

Discussion

In this study, we investigated the incidence of T1D in Northern Cyprus. According to our results, we can conclude that the mean annual incidence is intermediate (11.1/100000) in children and adolescents aged 16 or younger (10). In our country, there is only one study reflecting the incidence of T1D which was taken place in Southern Cyprus (6). Our study is the first population-based report on this subject in Northern Cyprus.

The study which was performed in 2011 by Skordis N et al analyzed a 20-year data on the incidence of T1D in subjects aged 15 or younger in the Southern Cyprus Territory. In the first decade of the study, the incidence was reported as 10.8/100000, whereas the incidence was 14.4/100000 in the second decade of the study. Thus the authors concluded that the incidence of T1D was rising (6). Our results were not compatible with these findings. In our study we report that between 2001-2005 the mean incidence rate was 11.2/100000; between 2006-2010: 11.4/100000 and between 2011-2016: 10.8/100000. Thus, the distribution of incidences was balanced among the years.

Northern Cyprus has close relations with Turkey and immigration in both directions is not rare. A prospective study which was published recently in Turkey calculated the mean crude annual incidence of pediatric T1D as 8.99/100000 between 2013 and 2015 (2). A retrospective study analyzing the incidence of T1D in children 14 or younger, in Southeast Turkey calculated the mean incidence as 7.2/100000 (3). A nationwide study involving 17175 prevalent cases of T1D subjects younger than 18 years calculated the age-standardized incidence rate as 10.8/100000 (95% CI, 10.1-11.5) in Turkey (10). Our figures are between those of South Cyprus and Turkey.

Cyprus is an island located in the Mediterranean Sea. Climate has been previously argued to have an effect on the incidence rate of T1D. We compared our data with other Mediterranean countries having data on the incidence rate of T1D. In Eastern Sicily, the incidence rate of T1D was 10.1/100000 between 1989 and 1990, and 11.7/100000 between 1990 and 1994 (11). Our results are similar to the data reported from eastern Sicily.

In Malta, the mean annual incidence rate of T1D was 13.6/100000 between 1980 and 1987 (12), and 24.68/100000 between 2006 and 2010 in children aged 14 or younger. The authors calculated a mean annual increase in the incidence of T1D by 21.8% per year (13). Sardinia is an island which also has high figures. The mean incidence rate was reported as 38.8/100000 between 1989 and 1999 (14).

According to our data, the mean annual incidence rate was slightly higher in boys compared to girls. Previous studies have reported a male predominance in high incidence countries and a female predominance in low incidence populations. A study by Karvonen et al reported that 88% of low incidence populations were predominantly girls, and high incidence countries were predominantly boys (4). Data from Sardinia report a male/female ratio of 1.4 in Children aged 15 or younger (14). Our results were similar to the data reported in Southern Cyprus. They reported a male/female ratio as 1.06/1 (6).

The proportion of newly diagnosed T1D was highest in the 9-12 age group followed by the 5-8 age group. We reported the lowest incidence rate in the 0-4 age group. Our data is consistent with previous large scale studies. A Multinational study performed (DIAMOND Project) documented that 10-14-year-old children had the highest incidence rates (15). Data from Malta reported the highest incidence rate in children aged 5-9 years (5)

In our cohort, T1D was most frequently diagnosed in April, followed by March. The study reported by Skordis et al regarding Southern Cyprus reported a significantly higher incidence of T1D in cold months (November, December, January, February) compared to hot months (June, July, August, September) in the first decade of the study. Incidence rates in neutral months were similar to that of the cold months (6).

The highest mean annual incidence rate was in Famagusta and the lowest rate was in Kyrenia. Both districts have coasted to the Mediterranean Sea. The climates of both districts are similar. We were unable to explain the difference in incidence rates in these two districts.

Limitations of the study

All subjects are diagnosed and treated at a single center. Thus, the study is strong due to the inclusion of all subjects with type 1 diabetes mellitus. The retrospective format is the studies limitation.

Conclusion

We conclude that according to our data the incidence of T1D in children aged 16 or younger is intermediate in our country and is stable among years.

Authorship Contributions

Surgical and Medical Practices: Umut Mousa, Hasan Sav, Osman Köseoğluları, Serap soytac İnançlı, Nese Akcan, Ruveyde Bundak

Concept: Umut Mousa, Hasan Sav, Ruveyde Bundak

Design: Umut Mousa, Ruveyde Bundak

Data Collection or Processing: Umut Mousa, Hasan Sav, Osman Köseoğluları, Serap soytac İnançlı, Nese Akcan, Ruveyde Bundak, Ayse Sahin

Analysis or Interpretation: Umut Mousa, Ruveyde Bundak

Literature Search: Umut Mousa

Writing: Umut Mousa

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References

- 1- Atkinson MA, Eisenbarth GS. Type 1 diabetes: new perspectives on disease pathogenesis and treatment. *Lancet*. 2001 Jul 21;358(9277):221-9. Review. Erratum in: *Lancet*. 2001 Sep 1;358(9283):766.
- 2- Poyrazoğlu S, Bundak R, Yavaş Abalı, Önal H, Sarıkaya S, Akgün A et al. Incidence of Type 1 Diabetes in Children Aged Below 18 Years during 2013-2015 in Northwest Turkey. *J Clin Res Pediatr Endocrinol*. 2018 Nov 29;10(4):336-342. doi: 10.4274/jcrpe.0025. Epub 2018 May 23.
- 3- Demirbilek H, Özbek MN, Baran RT. Incidence of type 1 diabetes mellitus in Turkish children from the southeastern region of the country: a regional report. *J Clin Res Pediatr Endocrinol*. 2013;5(2):98-103. doi: 10.4274/Jcrpe.954.
- 4- Chen YL, Huang YC, Qiao YC, Ling W, Pan Y, Geng L et al. Climates on incidence of childhood type 1 diabetes mellitus in 72 countries. *Sci Rep*. 2017 Oct 9;7(1):12810. doi: 10.1038/s41598-017-12954-8.
- 5- Casu A, Pascutto C, Bernardinelli L, Songini M. Type 1 diabetes among Sardinian children is increasing: Sardinian diabetes register for children aged 0-14 years (1989-1999). *Diabetes Care*. 2004 Jul;27(7):1623-9.
- 6- Skordis N, Efstathiou E, Kyriakides TC, Savvidou A, Savva SC, Phylactou LA et al. Epidemiology of type 1 diabetes mellitus in Cyprus: rising incidence at the dawn of the 21st century. *Hormones (Athens)*. 2012 Jan-Mar;11(1):86-93.

- 7- Sav H, Köseoğluları O, Taşyürek A, Kayımbaşıoğlu S, Özbalkıç S, Faiz M, Özyazar M. Redetermination of Diabetes, Impaired Glucose Tolerance and Related Factors among Turkish Cypriot Community. International Diabetes Federation, 20th World Diabetes Congress, 18-22 October 2009 Montreal, Canada, abstract book, p-1639, page 552.
- 8- <http://www.devplan.org/Frame-tr.html>
- 9- Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong CX et al. ISPAD Clinical Practice Consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents. *Pediatr Diabetes*. 2018 Oct;19 Suppl 27:7-19. doi: 10.1111/pedi.12773.
- 10- Yeşilkaya E, Cinaz P, Andıran N, Bideci A, Hatun Ş, Sarı E et al. . First report on the nationwide incidence and prevalence of Type 1 diabetes among children in Turkey.*Diabet Med*. 2017 Mar;34(3):405-410. doi: 10.1111/dme.13063. Epub 2016 Feb 12.
- 11- Chen YL, Huang YC, Qiao YC, Ling W, Pan YH, Geng LJ, Xiao JL, Zhang XX, Zhao HL. Climates on incidence of childhood type 1 diabetes mellitus in 72 countries. *Sci Rep*. 2017 Oct 9; 7(1):12810. doi: 10.1038/s41598-017-12954-8.
- 12- Schranz AG, Prikatsky V. Type 1 diabetes in the Maltese Islands. *Diabet Med*. 1989 Apr; 6(3):228-31.
- 13- Formosa N, Calleja N, Torpiano J. Incidence and modes of presentation of childhood type 1 diabetes mellitus in Malta between 2006 and 2010. *Pediatr Diabetes*. 2012 Sep; 13(6):484-8. doi: 10.1111/j.1399-5448.2011.00839.x. Epub 2011 Dec 13.
- 14- Casu A, Pascutto C, Bernardinelli L, Songini M. Type 1 diabetes among sardinian children is increasing: the Sardinian diabetes register for children aged 0-14 years (1989-1999). *Diabetes Care*. 2004 Jul; 27(7):1623-9.
- 15- Karvonen M, Viik-Kajander M, Moltchanova E, Libman I, LaPorte R, Tuomilehto J. Incidence of childhood type 1 diabetes worldwide. Diabetes Mondiale (DiaMond) Project Group. *Diabetes Care*. 2000 Oct; 23(10):1516-26.

Table 1: Distribution of the < 16-year aged population among districts according to the 2011 population survey in Northern Cyprus together with proportions and incidence rates among these districts

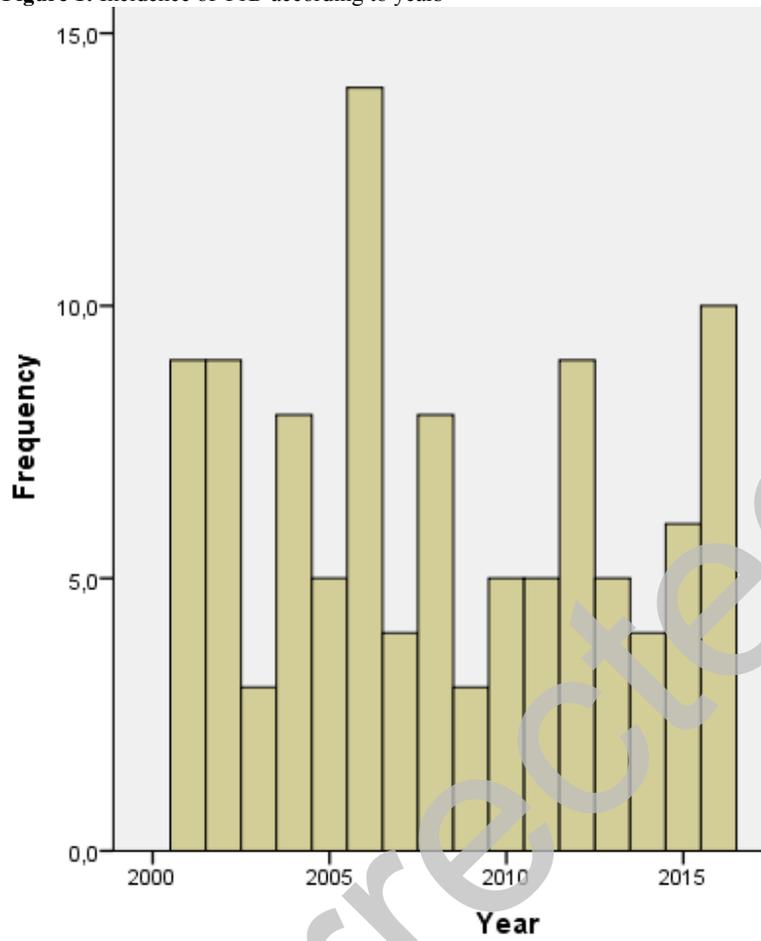
	Population n (%)	Incidence n (%)	Incidence rate(per 100000)
Nicosia	18889 (31.74%)	41 (38.3%)	13.5
Famagusta	14490 (26.67%)	33 (30.8%)	14.2
Kyrenia	13978 (23.17%)	13 (12.1%)	5.8
Guzelyurt	5654 (9.33%)	10 (9.3%)	11.1
Iskele	5392 (9.09%)	3 (7.5%)	9.2
Unknown	-	2 (1.9%)	-
Total	59315 (100%)	107 (100%)	11.1

Table 2: Proportions of newly diagnosed T1D according to age groups.

	N	%	Incidence rate/100000
4 years or younger	17	15.9	5.75
5-8 years	35	32.7	15.4
9-12 years	38	35.5	17.6
13-16 years	17	15.9	8.04
Total	107	100	11.1

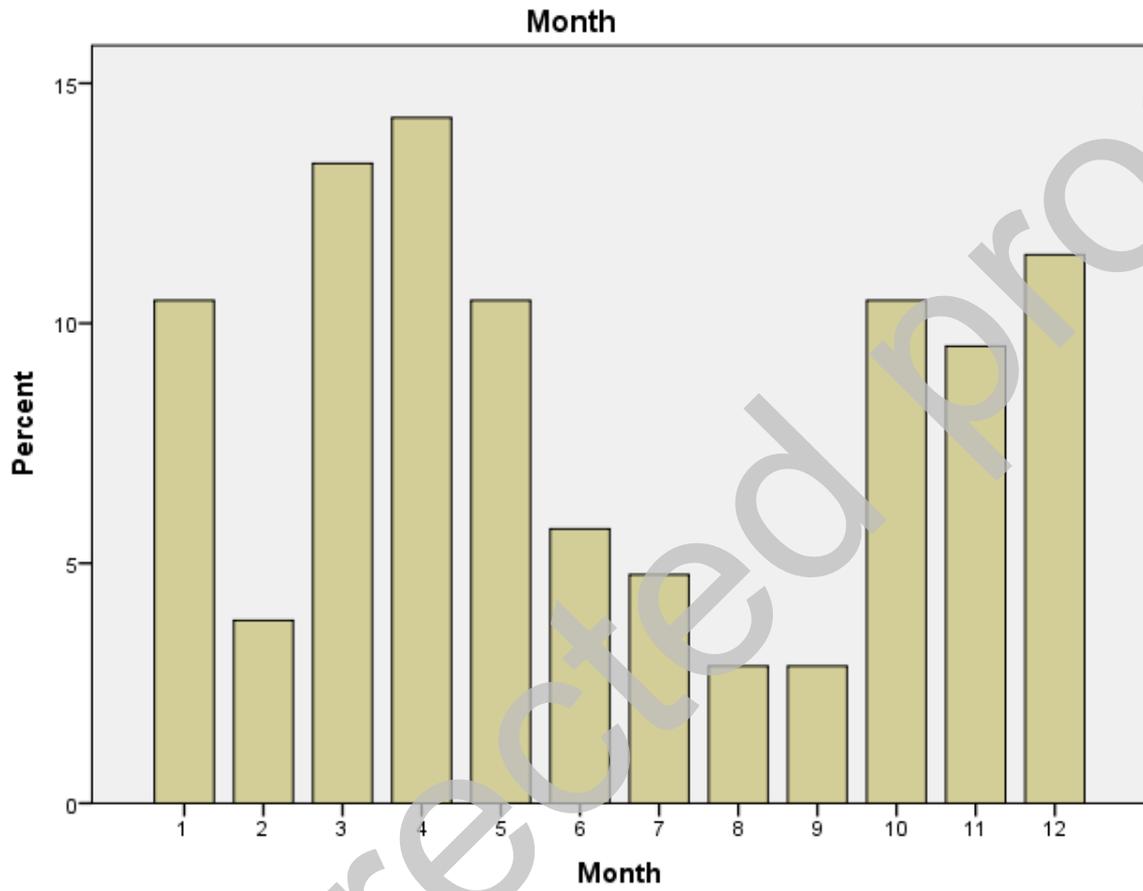
T1D: Type 1 diabetes mellitus

Figure 1: Incidence of T1D according to years



T1D: Type 1 diabetes mellitus

Figure 2: The diagnosis of T1D according to the month of diagnosis



T1D: Type 1 diabetes mellitus