

Original Article

A Survey on the Frequency of Type 1 Diabetes Mellitus and its Related Factors from 2004-2014

Moravej H¹, Rassafian M², Amirhakimi A², Ilkhanipour H², Mazloumi-abrazgah Sh², Yazdani N¹

1. Neonatal Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

2. Department of Pediatric Endocrinology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

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Abstract

Background & Objective: Since epidemiological information on type1 diabetes in children can help to control it, this study aimed to determine the frequency and characteristics of type1 diabetes patients during an 11-year period.

Materials & Methods: In this retrospective study, records of all 0-39 years old diabetic patients admitted to Nemazee hospital 2004-14 were reviewed. Since most new cases are admitted to this hospital, the patient's data might be a good representative of all patients in Shiraz. Gender, date of birth, age of onset and associated diseases were recorded. Data were analyzed, using SPSS 22.0.

Results: In this study, 546 diabetes patients were admitted, of which 52.4% were females. Two peak age was observed (5-9 Y/O and 10-14 Y/O). The mortality rate was 23%. Most of them had no family history of diabetes. Majority of patients (86.3%) did not have any other medical condition. Moreover, there was a significant relationship between age of onset with positive family history and mode of presentation. The frequency of diabetic patients had a rising trend during this eleven-year period.

Conclusion: Incidence of type1 diabetes had a growing trend and peak age of presentation was similar to most previous studies. However, the percentage of diabetic ketoacidosis was more than that of developed countries. Therefore, people and physicians are recommended to have more information on type1 diabetes for early diagnosis to prevent further complications.

Keywords: Diabetes Mellitus, Type 1, Diabetic Ketoacidosis, Epidemiology

Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by impairment in the metabolism of carbohydrates, lipids and proteins (1). Type 1 DM is characterized by insulin deficiency and a tendency to develop

ketosis, whereas type 2 DM is a heterogeneous group of disorders characterized by various degrees of insulin resistance, impaired insulin secretion, and excessive hepatic glucose production (2). There is a worldwide increase in the incidence of type 1 DM. In the past two decades, the global prevalence of diabetes has increased significantly from 30 million in 1985 to 382 million in 2013. According to the current International Diabetes Federation, it is estimated

*Corresponding Author: Yazdani Negar, Neonatal Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
Email: Yazdani.n2017@yahoo.com
<https://orcid.org/0000-0003-3720-7657>

that by the year 2035, 592 million people will be afflicted (2-4). The DIAMOND project was initiated by the World Health Organization (WHO) in 1990 to address the public health implications of type 1 DM to describe the incidence of T1D in children. An initial report in 2000 described the incidence of type 1 DM in children ≤ 14 years old (Y/O) in 50 countries, totaling 19164 cases from a population of 75.1 million children, an estimated 4.5% of the world's population 1990-99. Greater than 350-fold difference in the incidence of type 1 DM amongst 100 people worldwide was reported with age-adjusted incidences ranging from a minimum of 0.1/100000 per year in China and Venezuela to a maximum of 36.5/100000 in Finland and 36.8/100000 per year in Sardinia. The lowest incidence ($< 1/100000$ per year) was reported in China and South America and the highest incidence ($> 20/100000$ per year) was reported in Sardinia, Finland, Sweden, Norway, Portugal, the UK, Canada, and New Zealand (5). The highest incidence was related to two age groups of 4-6 Y/O and 10-14 Y/O (the early stage of puberty) (6). Although studies have shown that type 1 diabetic patients are not well controlled, it can also lead to complications, such as cardiovascular disorders and kidney problems even in adolescence (7,8). There is inadequate epidemiologic information on the prevalence of diabetes in Iran, but a study was conducted in Fars province 1991-96, indicating that there was a low prevalence of diabetes in Iran in comparison with the rest of the world (9). Due to the high prevalence of type 1 DM in the world, it's importance on the quality of life and longevity, and its effects on patients' personal and social life, collecting information on this issue is of great importance. In Shiraz, all newly diagnosed type 1 diabetic patients are admitted to Nemazee hospital for insulin therapy; hence their data is a good representative of all patients in Fars province. In the present study we aimed to determine the frequency and characteristics of type 1 diabetes patients during an 11-year period.

Materials & Methods

In this retrospective study, all type 1 diabetic patients who were admitted to Nemazee Hospital, Shiraz, Iran 2004-14 were included *via* census method. The information was extracted from the patient's records.

At first, the patient's name and case number were written on a card. Next, the patients' records were used to extract the necessary information including age, gender, place of residency, family history of diabetes, associated illness and the mode of presentation (diabetic ketoacidosis (DKA), non-DKA). The inclusion criteria were patients who had type 1 DM, age range 0-39 years and having complete patients' records. The patients with corticosteroid consumption, known as the case of organ transplant with incomplete patients' record, and patients and patients over 39 years of age were excluded.

Statistical Analyses

The Statistical Package for the Social Sciences software (SPSS: An IBM Company, version 18.0, IBM Corporation, Armonk, NY, USA) was used for data analysis. Demographic data are summarized, using descriptive statistics (Mean and Standard Deviation, and frequency). Moreover, analytic data were analyzed by t-test, ANOVA, and Chi-square test. P-value < 0.05 was considered to be statistically significant.

Results

In this study, amongst 546 patients, 286 (52.4%) were females. The mean age of the participants was 12.43 years old (0-39 Y/O), of which 476 (87.18%) were less than 20 Y/O, and 70 (12.82%) were older than 20 Y/O. The mean age at the disease onset in females was 12.65 years and in males was 12.22 years, although not significant. Table 1 shows the age distribution of samples based on gender and type of diabetes.

Two identified age peaks were 5-9 Y/O and 10-14 Y/O. Amongst the samples 316 (57.9%) patients lived in Shiraz, and 230 (42.1%) lived in Fars counties.

The incidence of diabetic showed a growing trend during 2004-14, including 32 (5.86%), 41 (7.50%), 39 (7.14%), 46 (8.42%), 50 (9.15%), 51 (9.32%), 58 (10.62%), 52 (9.52%), 56 (10.25%), 63 (11.53%), and 58 (10.62%).

Our results showed that 267 participants (48.9%) had a family history of diabetes, of which 59 (22.09%) had a family history of type 1 DM, 200 (74.90%) patients had a family history of type 2 DM, 8 (2.99%) of them had a family

Table 1. Age Distribution of the Samples based on Gender and Type of Incidence of Diabetes

Age group	n (%)	Gender(%)		Type of Incidence(%)	
		Male	Female	DKA	Non-DKA
0-4	48 (8.8)	22 (4)	26 (4.8)	50 (9.2)	42 (7.8)
5-9	152 (27.8)	72 (13.2)	80 (14.7)	158 (28.9)	136 (25.3)
10-14	199 (36.4)	93 (17)	106 (19.4)	204 (37.4)	187 (34.3)
15-19	77 (14.1)	35 (13.5)	42 (14.7)	77 (14.2)	75 (13.9)
20-24	25 (4.6)	13 (2.4)	12 (2.2)	21 (3.9)	32 (6)
25-29	26 (4.8)	16 (2.9)	10 (1.8)	20 (3.7)	39 (7.2)
30-34	12 (2.2)	7 (1.3)	5 (0.9)	8 (1.6)	19 (3.6)
35-39	7 (1.3)	7 (1.3)	0 (0)	5 (1)	9 (1.8)

Table 2. The Relationship between Different Diabetic-Related Factors with Types of Diabetes and Other Factors

Related Factors	P-value	
Age of onset of disease	Mode of Presentation	0.004
	Gender	0.40
	Family History	0.019
Negative Family history	Type 1 Diabetes Mellitus	0.03
	Type 2 Diabetes Mellitus	0.02
	Pregnancy Diabetes Mellitus	0.22
Diabetes Mellitus type 1	Type 2 Diabetes Mellitus	0.54
	Pregnancy Diabetes Mellitus	0.05
Gender	Mode of Presentation	0.46
	Family History	0.50
	Associated Disease	0.37
Mode of presentation	Family History	0.96
	Associated Disease	0.005

history of gestational diabetes, and 279 (51.1%) had no family history of diabetes. Moreover, patients with a positive family history of type 1 and 2, and gestational diabetes mainly showed the incidence of diabetes in the age groups of 1 to 5, 10 to 14, and 15 to 19 Y/O, respectively.

The present study indicated that 33 (6.04%) of the patients with type1 DM had at least one first-degree family with type1 DM, and 26 (4.76%) of type 1 DM had at least one second-degree family with type1 DM.

Our findings indicated that 380 (69.6%) patients reported the DKA for the first time and 166 (30.4%) patients first reported the disease as non-DKA.

Amongst the studied population, 435 (79.67%) had no associated diseases. Also, 111 (20.32%) patients had one associated disease, such as Celiac (2.6%), Hypothyroid disorder (4%), Asthma (0.4%), and Down Syndrome (0.9%).

Amongst our samples, 19 (3.50%) had macrovascular complications of diabetes

including Brain vascular disease, hypertension and coronary artery disease, and 14 (2.60%) patients had microvascular complications of diabetes, such as retinopathy, neuropathy and nephropathy.

Based on the results, 23 out of 546 (4.21%) patients died, of which 14 (60.86%) cases were due to DKA and its complications, two (8.69%) cases due to pancreatic cancer, 4 (17.39%) cases due to kidney failure and its complications, such as Double Lumen infection, one (4.34%) case due to macrovascular illnesses, one (4.34%) case due to hypoglycemia, and one (4.34%) case due to complications of cystic fibrosis (CF).

Also, 513 (94.1%) patients were diagnosed with polyuria and polydipsia during the first visit.

Statistical test showed that there was a significant relationship between different diabetic-related factors, such as the age of the onset with a positive family history of diabetes and mode of presentation ($P < 0.05$). Similarly, the family history had a significant relationship

with type 1 and type 2 diabetes ($P < 0.05$), but there was no significant relationship with gestational diabetes ($P > 0.05$). Furthermore, mode of presentation had a significant relationship with the associated diseases ($P < 0.05$). There was no significant relationship between the incidence of diabetes and gender ($P = 0.46$) (Table 2).

Discussion

In this retrospective study, we evaluated the characteristics of type 1 diabetic patients admitted to Nemazee Hospital, Shiraz, Iran 2004-14 based on age, gender, place of residency, mode of presentation, family history of diabetes, and associated illness. According to the result, the incidence of type 1 DM in children is on the rise. Similarly, a study conducted in 17 European countries 1989-2003 showed 3.9% increase in the incidence of diabetes among children. If the present trend continues, the doubling of new cases in European children younger than 5 years is predictable, and cases younger than 15 years will rise by 70% (10). Hence, it is recommended that policymakers come up with a strategy for early diagnosis of DM in children to prevent the progression of DM during their adulthood.

In the present study, two peaks were observed in the age range of 5-9 years and 10-14 years. Since the school entry age in Iran is 6 years and puberty is approximately 10-14 years, these peaks are consistent with the global age range of the onset for type 1 DM. The peak onset of type 1 DM in two age groups is 5-7 years and puberty. The first peak is proportional to the time of exposure to infections at school, and the second peak is proportional to peak growth and maturation and growth hormone secretion (3).

Our findings revealed no significant difference in type 1 diabetic patients between males and females. A study in Lithuania 1991-2008 on 15-34 years-old with type 1 DM showed that the frequency of diabetic boys was significantly higher than girls (11). On the other hand, according to world statistics, boys and girls are almost equally affected by type 1 DM, but in some lower-risk populations, such as Japan, the disease is predominant amongst girls (3). In a study in Fars province (1991-96), the annual incidence of type 1 DM amongst girls 0-29 years was 4.26/100000 cases per year, and the incidence of type 1 DM amongst boys 0-29 years

old was 3.36/100000 case per year (9). According to this statistical difference, it can be concluded that in addition to gender, other factors, such as place of residency, genetics, and environmental factors in different regions of the world might lead to different statistics on the annual incidence of type 1 DM.

In our study, 94.1% of diabetes cases had presentations of polydipsia and polyuria symptoms at the time of diagnosis during their first visit. This result is in line with another study in Turkey (2015), which revealed that 94.7% of people with type 1 DM were diagnosed with polydipsia and polyuria for the first time (12). Therefore, it can be concluded that polydipsia and polyuria are the most common symptoms of patients with type 1 DM. Polydipsia and polyuria are caused by the excretion of sugar from the kidneys and the excretion of large amounts of water following sugar that results in a person becoming regularly thirsty, leading to drinking too much water.

Also, the present study showed a significant relationship between the age of incidence and mode of DM presentation. As the age of onset is increasing, there is a change in the presentation of diabetes. On the other hand, with increasing age, the likelihood of DKA decreases and the form of non-DKA increases. But another study conducted in 2010 showed that there was no significant correlation between age and the occurrence of DKA in children (13). DKA can also occur in 20-40% of children at the onset of diabetes (3). On the contrary, in the present study, the percentage of people with type 1 DM who had diabetes with DKA was higher than in other studies. This can be related to people's lack of awareness of the symptoms and late referral for treatment.

Our findings showed that a significant relationship existed between the age of onset and family history. Almost half of our samples had a family history of three types of diabetes (type 1 and 2 diabetes and gestational diabetes). Amongst them, 6.04% of the people with a family history of type 1 DM had at least one first degree family member with type 1 DM and 4.76% of people with a family history of type 1 DM had at least second-degree family member with type 1 DM. In this regard, a study conducted in Finland (2013) showed that 12.2% of children with type 1 DM had at least one first degree family member with type 1 DM and 11.9% of children with type 1 DM had at least one second-

degree family member with type 1 DM (14). This indicates the positive impact of family history on the diabetic patients. Although the prevalence of family history in type 1 diabetic patients in this study was consistent with our results, they did not report the percentage of patients with a family history of type 2 DM. However, a study on Iraqi children and youth with type 1 DM, found that family history of type 1 DM in the first and second-degree relatives was a risk factor that was unrelated to the risk of developing type 1 DM in patients (15). The statistical difference between the two studies can be related to various causes, such as incomplete patients' history or the influence of other causes including place of residence, genetics, and environmental factors.

Also, 22 (4%) of our samples had hypothyroidism. A 2016 study in Taiwan found that children and adolescents with type 1 DM were significantly more likely to develop thyroid diseases than healthy controls. Goiter probability was 2.74%, hypothyroidism 16.07% and hyperthyroidism 6.64% (16). Two to five % of patients with type 1 DM develop autoimmune hypothyroidism. Since the prevalence of autoimmune thyroiditis amongst girls is higher than boys and increases with age, screening all children with type 1 DM should be performed regularly with TSH measurements (17,18). Even though the number of people with hypothyroidism in this study was equal amongst both genders, the likelihood of hypothyroidism was similar to previous studies.

Long-term complications can be divided into two categories: microvascular, such as retinopathy, nephropathy and neuropathy and macrovascular, such as coronary artery disease, peripheral vascular disease and cerebrovascular diseases (19). In this study, 19 patients had macrovascular complications, of which eight had diabetic nephropathy and 14 patients had microvascular complications. The pathogenesis of these complications starts when the disease begins. Clinical evidence of these complications is rarely seen in children and adolescents. Diabetic nephropathy is a well-known cause of advanced kidney disease in the United States. It affects 20-30% of the patients with type 1 DM at the time of onset. The average 5-year survival for diabetic end-stage renal disease (ESRD) is less than 20%. As a result, screening for diabetic nephropathy should be a routine aspect of diabetic care (3). According to statistics reported by the American Diabetes Association (ADA) in

2013, during the years 2009-12, 71% of people older than 18 Y/O had blood pressure more or equal to 140/90 or took antihypertensive drugs. During 2003-06, mortality rates from cardiovascular disease in diabetic patients over 18 Y/O was 1.7 times higher than those without diabetes. In 2010, the number of people with diabetes older than 20 Y/O hospitalized for stroke was 1.5 times higher than non-diabetics. Based on statistic results, 4.2 million (28.5%) diabetic patients older than 40 years of age suffered from blindness and visual problems due to diabetic retinopathy during 2005-08. In 2011, diabetes was considered as the leading cause of kidney failure in 44% of newly diagnosed patients (20).

In our study, 14 patients had celiac disease, of which three were male and 11 were female. According to another study, almost 4.5% of people with type 1 DM develop the celiac disease (21). The incidence of celiac disease among children with type 1 DM in the first 6 years of life is 7-15%. Also, it is more common among children younger than 4 years and also girls (3). In this study, similar to previous research, the prevalence of celiac between girls was more common than boys. The incidence rate was 2.9%, which is lower than in previous studies.

Strengths and limitations

There were two limitations to the present study. Importantly, the current study was performed only in Shiraz and Fars counties; hence, the results cannot be generalizable to other populations. A final limitation was that most samples were missed due to incomplete recode or lack of medical history.

Despite the aforementioned limitations, most of the new type 1 DM cases are admitted to Nemazee hospital, which might be a good representation of the diabetic population in Shiraz, Fars province, which shows the power of our sampling.

Therefore, it is suggested to conduct other studies with larger samples in other cities on factors that had a significant relationship, since it can help to prevent the incidence and progressing of type 1 DM.

Conclusions

There is a growing trend in the incidence of type 1 DM, and the peak presentation was the same as other studies. However, the percentage of diabetic ketoacidosis was more than that of developed countries. Therefore, people and

physicians are recommended to have more information on type1 diabetes to diagnose it early, prevent its complications, and access to this information will facilitate planning for future services.

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Conflict of Interests

The authors declare no conflicts of interest.

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مقاله پژوهشی

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حسین مروج^۱، مرضیه رصافیان^۲، انیس امیرحکیمی^۲، هما ایلخانی پور^۲، شکرالله مظلومی آبرزگاه^۲، نگار یزدانی^{۳*}

۱. مرکز تحقیقات نوزادان، دانشگاه علوم پزشکی شیراز، شیراز، ایران

۲. بخش غدد اطفال، دانشکده پزشکی، دانشگاه علوم پزشکی شیراز، شیراز، ایران

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چکیده

زمینه و هدف: از آنجاییکه اطلاعات اپیدمیولوژیک در مورد بیماری دیابت نوع ۱ در کودکان می‌تواند در کنترل آن کمک کند، این مطالعه با هدف تعیین فراوانی و ویژگی‌های مهم بیماران مبتلا به دیابت نوع ۱ در یک دوره ۱۱ ساله انجام شد.

مواد و روش‌ها: در این مطالعه گذشته نگر، پرونده کلیه بیماران دیابتی ۳۹-۰ ساله بستری شده در بیمارستان نمازی بین سال‌های ۱۳۸۲ تا ۱۳۹۲ مورد بررسی قرار گرفتند. از آنجاییکه بیشتر موارد جدید در این بیمارستان پذیرش می‌شوند، داده‌های حاصل از بیماران این بیمارستان می‌تواند نماینده خوبی از داده‌های همه بیماران شیراز باشد. جنسیت، تاریخ تولد، سن شروع و بیماری‌های مرتبط با دیابت ثبت شد. داده‌ها با استفاده از نرم افزار SPSS نسخه ۲۲ تجزیه و تحلیل شدند.

نتایج: در این مطالعه ۵۴۶ بیمار مبتلا به دیابت در بیمارستان بستری شده که ۵۲/۴٪ آنها زن بودند. دو سن اوج مشاهده شد (۹-۵ و ۱۴-۱۰ سال). آمار مرگ دیابت ۲۳٪ بود. در اکثر نمونه‌ها سابقه خانوادگی انواع مختلف دیابت وجود نداشت. ۸۶/۳٪ بیماران هیچ بیماری همراه نداشتند. همچنین بین سن شروع بیماری با سابقه خانوادگی مثبت بیماری دیابت و نحوه ارائه بیماری رابطه معنی‌داری مشاهده شد. تعداد بیماران دیابتی در طول دوره یازده سال روند رو به رشدی داشت.

نتیجه‌گیری: بروز بیماری‌های دیابت نوع ۱ روند رو به رشد داشته و سن اوج بیماری مشابه اکثر مطالعات قبلی است. به هر حال درصد کتواسیدوز دیابتی بیشتر از کشورهای توسعه یافته بود. بنابراین افراد و پزشکان به کسب اطلاعات بیشتر برای تشخیص سریع‌تر دیابت نوع ۱ و جلوگیری از عوارض آتی توصیه می‌شوند.

کلمات کلیدی: دیابت ملیتوس، نوع یک، کتواسیدوز دیابتی، اپیدمیولوژی

*نویسنده مسئول: نگار یزدانی، مرکز تحقیقات نوزادان، دانشگاه علوم پزشکی شیراز، شیراز، ایران.

Email: Yazdani.n2017@yahoo.com
https://orcid.org/0000-0003-3720-7657