

*Original Article***The prevalence of type 1 diabetes in children of Mazandaran province**Daniel Zamanfar<sup>1</sup> **Pooneh Yazdani**<sup>2\*</sup> Mohsen Aarabi<sup>3</sup> Hedieh Pournorooz<sup>4</sup>

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(Received: 13 Jan. 2018; Revised: 24 Feb. 2018; Accepted: 4 Apr. 2018)

**Abstract**

**Background and purpose:** The prevalence of type 1 diabetes in all countries throughout the world is different. In this study, an introduction is, therefore, provided for the development of type 1 diabetes in children in Mazandaran province by using all available resources.

**Methods:** In this descriptive cross-sectional study, the prevalence of patients with initial diagnosis of type 1 diabetes mellitus, aging from 6 months to 18 years, was located through contacting and referring to all organizations of insurers and doctors or experts in children endocrinologist and adolescent diseases in Mazandaran province.

**Results:** 289 patients with type 1 diabetes were identified, 138 of whom were male (47.8%), and 151 were women (52.2%) with an overall prevalence of 0.04%, and the rate of this prevalence was 48 cases among 100000 people (50 cases among 100000 girls and 36 cases among 100000 boys). The mean age of the patients was 11.5 years old. In the study of delivery method, 180 patients (62.3%) were diagnosed with cesarean section, and 109 (37.7%) were born through natural delivery method. The mean age of onset of diabetes was 7 years. The minimum and maximum ages were 7 months and 18 years, respectively. 97 (33.6%) of the patients were also hospitalized for the first time due to ketoacidosis, and were diagnosed with diabetes.

**Conclusion:** Type 1 diabetes in Mazandaran province was more prevalent than the similar study in southern Iran and neighboring countries. It is essential to pay greater attention to this disease through studying it in the other parts of the country.

**Keywords:** Type 1 diabetes; Prevalence; Pediatrics; Mazandaran

**Citation:** Zamanfar D, **Yazdani P\***, Aarabi M, Pournorooz H. The prevalence of type 1 diabetes in children of Mazandaran province 2018; 6 (2): 1-10.

## **1. Introduction**

Diabetes is a metabolic disorder characterized by hyperglycemia due to impaired secretion or function of insulin, or both. Type 1 diabetes is also called diabetes-related insulin and diabetes, and is often due to the destruction of cellular autoimmune proteins in the pancreatic beta cells (1, 2). Epidemiologic studies define the onset of type 1 diabetes, since the first dose of insulin is injected. The prevalence of this disease may vary in different countries of the world, as well as different demographic segments. The prevalence of diabetes in Asia is significantly lower than in Europe (2). The highest prevalence rate is in Finland with a prevalence of 37 per 100,000 people under 15 years of age and Sardinia with a prevalence of 45 per 100,000 population under the age of 15. This prevalence is 400 times bigger than the prevalence in countries like Venezuela and some parts of China, which is 1 to 5 cases per 1,000,000 people under the age of 15 (3, 4). Also, in some populations, the difference in prevalence was seen in both sexes (5). The background studies have shown an increase in the incidence of this disease, and especially in less than 5 years of age, an increase in the incidence of illness (3). The highest incidence was related to two age groups of 4 to 6 years old and 10 to 14 years old (at the early stage of puberty), and 45% of the cases were under the age of 10 years. Seasonal variation has also been reported in new cases at the onset of the disease, and in the winter, new cases have been reported. Family history has also been considered as a contributing factor (4).

With an increase in childhood obesity, type-2 diabetes is also on the rise; however, type-1 diabetes is still the most

common type of diabetes in children worldwide. There is not enough epidemiological information about the prevalence of type 1 diabetes in Iran, although this type of information is available in most countries (4). Given the high prevalence and the importance of the disease in the quality of life and longevity of patients, as well as the high cost of the individual and society, and the prevalence and incidence of the disease in different parts of the world, and the lack of information on type 1 diabetes in children in Mazandaran province, it is necessary to gain access to the existing data in this field. Therefore, in the present study, we intend to introduce an introduction system for the registration of type 1 diabetes in children in Mazandaran province using all available resources. Considering that all of these patients use insulin to control their blood glucose, and insulin coverage by health insurance organizations is subject to registration of patient profiles, all available information sources were used in this study to determine the total number of patients and the outbreak of the disease. An all-encompassing registration system was developed as a suitable tool for recording follow-ups and long-term follow-ups of these patients. Obviously, access to this information will also facilitate planning for the provision of services in the future.

## **2. Method**

The study was a descriptive cross-sectional study, in which the prevalence of early diagnosis of type 1 diabetes mellitus was between the ages of six month and 18 years in Mazandaran province (except for the covered areas of Babol University of Medical Sciences). By contacting and referring to all health insurance

organizations and doctors of endocrine diseases, as well as rural and urban health centers of the province, type 1 diabetes patients were identified, and their characteristics were assessed after registration. In a letter explaining the goals of the plan that achieved the prevalence of a comprehensive system for registering patients with type-1 diabetes in Mazandaran province, the patients were contacted by associate doctors of pediatric and adult endocrinologist. In case of non-response, follow-up was also done to obtain the required information. Name and contact details of type-1 diabetes patients receiving insulin were recorded in coordination with the basic insurance organizations (Mazandaran Health Insurance, Social Security Organization, Armed Forces Insurance, Imam Khomeini Relief Committee). The list of patients received from different sources was also adapted to prevent recurrence of patient data. The sources of all data were medical doctors or the highest healthcare professionals working in those centers. Finally, the records of all of these people were examined and the age, sex, height, weight, place of birth and residence, age of the onset of illness, the season of the onset of the illness, absence or presence of type 1 diabetes in parents, presence or absence of family history, presence or absence of simultaneously hybrid thyroid disease, and other information from the patients' files were collected. In addition, when in contact with the patients or their parents, the patients were invited to visit and receive the required data based on a pre-designed checklist.

The criteria for entering the study included: the age of onset of diabetes between 6 months to 18 years, the onset of the disease with the DKA panel, the

presence of Anti-GAD65 positive antibodies, and other specific antibodies to diabetes, and reduction of C-peptide and insulin-dependent treatment. Having the positive antibody of AntiGADS65 and other exclusive antibodies of diabetes in the province over the past 2 years, antibody positivity has been suggested as a strong criterion, but since about 10% of patients have antibody negative, patients with other diagnostic conditions and antibodies negative as a result of being unmeasurable were also considered as type 1 diabetes. Also, exclusion criteria included: the age at which the disease started had to be less than 6 months and more than 18 years, the syndrome associated with diabetes (Turner-Down ...), type-2 diabetes, MODY-pharmaceutical, and Thalassemia. Finally, the collected data for each patient were examined by a doctor specializing in endocrine and metabolic diseases of children. If the diagnosis was confirmed by them, the person was enrolled as a type 1 diabetic patient. This study has been completed with ethics code: 930. SPSS Software version 16 and descriptive statistics were used to describe the data. To calculate the prevalence of a population between the age of six month and 18 years old, the census was used as the denominator in the last population and housing census of the country. In order to achieve geographical distribution, the prevalence rate was also calculated in each county or region.

### **3. Results**

In this study, 325 patients with type 1 diabetes were identified. 36 patients were excluded from the study due to being above the age range, and 289 patients with type 1 diabetes were studied. Of these 289

people, 138 were men (47.8%) and 151 were women (52.2%). The mean age of patients in the study was 11.5 years (95% confidence interval 11 to 12.0). The mean age of men in this study was also  $11.47 \pm 3.94$ , and the mean age for women was  $11.61 \pm 4.13$ , which was not significantly different between the two groups ( $P=0.761$ ). During this period, all persons between 6 months and 18 years old living in Mazandaran province (except for the covered areas of Babol University of Medical Sciences), who were calculated at the last census of population and housing, were used as a denominator. It turned out that 601,812 people were in this age range. Also, in the gender segregation of these individuals, it was found that 380,146 were men and 293,666 were women. Eventually, the overall prevalence of this disease was found to be 0.04% and 48 per 100,000 people, with an estimated 50% per 100,000 in women and 36 in 100,000 in men.

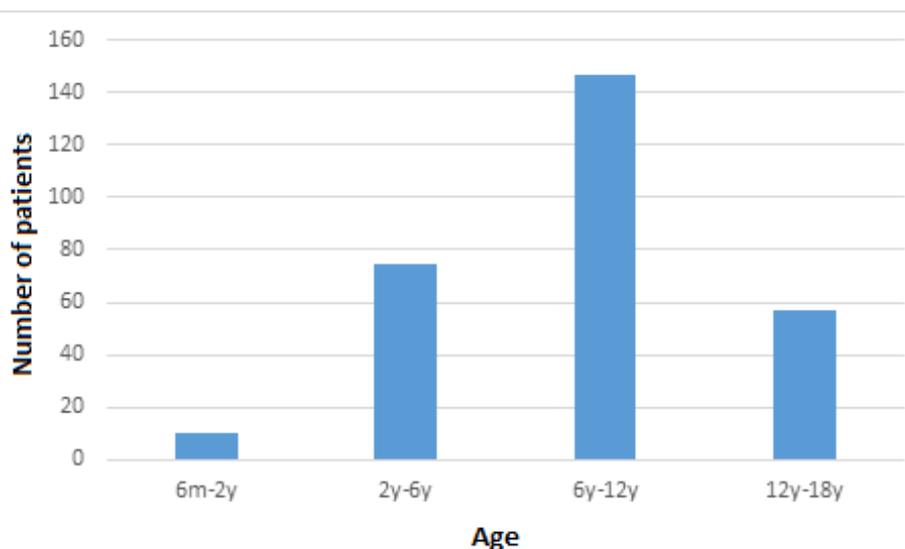
In the questionnaire prepared for each patient, the gestational age was recorded. The mean of gestational age at birth was 37.4 weeks (95% confidence interval 37.2 to 37.7), and the mean of gestational age in boys was  $37.84 \pm 1.92$  weeks, while it was  $37.39 \pm 2.02$  in girls. Hence, the difference between boys and girls was not statistically significant ( $P=0.704$ ). Also, the average birth weight was 3146 g (95% confidence interval 3080 to 3211 g), and the mean weight of boys was  $627.48 \pm 3155.289$  g, whereas this quantity was  $506602 \pm 31370.08$  g for girls. Hence, there was no significant difference between boys and girls in this study ( $P=0.786$ ).

At the same time, the method of delivery was recorded for each patient in the current study, and it was found that 180 patients (62.3%) give birth in cesarean section,

while 109 patients (37.7%) experienced natural delivery method. The difference between the method of delivery in boys and girls was not statistically significant ( $P=0.799$ ).

Regarding breastfeeding, the average period was 20.4 months (95% confidence interval: 19.6 to 21.2 months). The average breastfeeding time for boys was  $6.21 \pm 20.84$  months, and for girls it was  $7.19 \pm 19.97$  months, which showed not any statistically significant difference ( $P=0.269$ ). It was also found that 43 patients (14.87%) used milk formula. The average duration of diabetes in patients who consumed milk formula was  $7.73 \pm 3.7$  years, and in patients who used breast milk, the duration was  $3.81 \pm 7.4$  years. In a survey conducted between two groups of opinions, there was found no statistically significant difference in the onset of diabetes based on breast milk and milk formula ( $P=0.428$ ). The mean age of the beginning of the cow's milk was 15.9 months, and the median was 16 months. In the boys' individual examination, the mean age of the beginning of cow's milk was  $15.59 \pm 8.34$  months, and in girls, it was  $16.19 \pm 8.12$  months, which again showed not any statistically significant difference between the two groups ( $P=0.457$ ).

The mean age of onset of diabetes in this study was recorded to be 7 years, with a median of 6 years and a 95% confidence interval. Also, the patients were 6.5 to 7.4 years old in type 1 diabetes onset (Figure 1). The minimum and maximum age was 7 months and 18 years old, respectively. Also, the mean age of boy patients was  $6.77 \pm 3.77$  years and girl patients was  $7.66 \pm 3.66$  years that the difference between boys and girls was not statistically significant ( $P=0.319$ ).



**Figure 1.** The age of onset of type 1 diabetes in the patients

Of the 289 patients in the study, 97 (33.6%) patients were hospitalized for the first time due to ketoacidosis, and were diagnosed with diabetes, of which 47 (48.4%) were boys and 50 (51.6%) were girls. The findings showed that there was no significant relationship between the onset

of diabetes and ketoacidosis and gender ( $P=0.715$ ). Twenty-eight patients, in addition to having diabetes, have also been referred to a related illness, of which 14 patients (44.8%) were girls and 14 patients (52.8%) were boys (Table 1).

**Table 1.** Prevalence of comorbid diseases in patients of type 1 diabetes

Frequency of diseases		Boys	Girls	Total
<b>Allergy</b>	Number	2	1	3
	Percentage	1.4%	0.6%	1%
<b>Asthma</b>	Number	2	1	3
	Percentage	1.4%	0.6%	1%
<b>Celiac</b>	Number	6	3	9
	Percentage	4.2%	1.9%	3.1%
<b>Hypothyroidism</b>	Number	3	4	7
	Percentage	2.2%	2.6%	2.4%
<b>Hyperthyroidism</b>	Number	1	3	4
	Percentage	0.7%	1.9%	1.3%
<b>Vitiligo</b>	Number	0	2	2
	Percentage	0%	1.3%	0.7%

In patients' history, it was found that 67 patients (23.2%) had had a history of diabetes in their family, while 62 patients had experienced a history of type 2 diabetes in their own families. The whole

information is available in Table 2, and it was observed that there was no significant difference between girls and boys in the survey ( $P=0.324$ ).

**Table 2.** History of diabetes in the family of patients categorized by gender and type

Frequency of diseases in the family		Patients with Type 1 Diabetes by gender		Total
		Boys	Girls	
Type 1	Number	3	2	5
	Percentage	2.2%	1.3%	1.7%
Type 2	Number	25	37	62
	Percentage	18.1%	24.5%	21.5%

#### 4. Discussion

In this study, 289 patients with type 1 diabetes were studied. Of these 289, 138 were men (47.8%), and 151 were women (52.2%) (6). In the current research, the prevalence of type 1 diabetes was found to be 0.04% and 48 patients per 100,000. In a study by Dana Dabelea et al. in the United States, the prevalence of type-1 diabetes in children was also calculated. The study found that the prevalence of type 1 diabetes was different regarding race and gender. The most commonly reported outbreak in white patients was the prevalence of 255 per 10,000 people and the lowest among American Indians with 0.35 per 10,000 people (7). A study in Iran, found that the incidence of diabetes in Iran was about 37 per 100,000, while in a country like Kuwait this figure was 18.3 per 100,000, and In Russia, this figure was reported to be 6 per 100 000 people (8). Also, in the study of Rakhimova in Uzbekistan, the prevalence of type 1 diabetes roughly doubled over 1998-2014 (7.8 to 15.3/100,000 population

aged <15 years), following a doubling of incidence (1.5 to 3.1/100 000 <15 years, a 5.6% annualized increase). Also, there was a female preponderance, with a male/female ratio of 0.89 (9). Based on the findings of the current study, the dependence of type-1 diabetes on the prevalence of the disease in northern Iran is higher than that of neighboring countries.

In the present study, 34% of the patients were hospitalized for the first time due to ketoacidosis, and were diagnosed with diabetes. However, in the various studies worldwide, the highest frequency of detection of type-1 diabetes is based on ketoacidosis in UAE (80%), Romania (67%), Taiwan (65%), and Saudi Arabia (59%) and the lowest In Sweden (14%), Canada (18.6%), Finland (22%) and Hungary (23%) (10), which indicates various differences in these statistics. It is, thus, documented that there is statistically a better ratio in our region than the rest of Asia, but still specific measures need to be taken to reduce this rate, such as education through mass media to families about type-

1 diabetes symptoms, and surveys of people with a family history of type-1 diabetes.

In the present study, 48% of the patients were men and 52% were women with an average age of 11.5 years, with a slightly higher, but almost identical, frequency of women. In a study conducted by Moussa, the maximum prevalence of disease was reported in the age range of 10-13 years, and the prevalence was more common in men (1 to 1.7) (11), which was found to be somewhat higher in our study. Meanwhile, in the United States in 2013, 51% were male and 49% were female (12). In other studies, there was no significant difference in the prevalence of men and women with age (13-15). Type 1 diabetes could then cause almost any degree of involvement in any of the two sexes and may sometimes be higher in women.

In the current study, the average breastfeeding period was 20.4 months, 15 percent of them used milk formula during their infancy. There was also no significant difference in the time of onset of diabetes based on breast milk and the infant formula. However, Sadauskaitė stated in his study in Sweden that breast-feeding for more than five months, or breastfeeding for more than seven months, or breastfeeding after the third month of birth, protects against type-1 diabetes, and children who have been implicated in breast-feeding are at high risk for type-1 diabetes (16). The Patelarou study also stated that short-term use or lack of breast-feeding may be a risk factor for type-1 diabetes (17).

Insulin-dependent diabetes is closely linked to other autoimmune diseases, including thyroid and skin diseases. Of all 5 children with insulin-dependent diabetes, one has anti-thyroid antibodies in his

serum, with a prevalence of 20-2 times higher than the typical population. In a case series study in 2001 in Tehran University, 122 patients with type-1 diabetes who referred to the Endocrinology and Metabolism Institute and the Office of the Institute of Endocrinology and Obstetrics and Gynecology were examined. The aim of this study was to determine the prevalence of goiter and thyroid disorders in diabetic children, and to determine the importance of examining these disorders in these patients. Complete history was taken from all patients, and physical examinations were carried out on all patients. At the same time, WHO categorization was used to determine the degree of goiter, and thyroid tests were done. The patients were in the age range of 2-16 years with an average age of 11.2 years and an average of 4.2 years of diabetes duration. 64 of the patients were female and 58 were male. The prevalence of goiter in patients was found to be 2.53% (65 cases), of whom 9 were hypothyroid patients and only two had hyperthyroidism, and 54 of them were euthyroid patients. The findings of this case series study indicated that the risk of goiter and thyroid diseases in patients with type-1 diabetes was higher than others (18). The results of our study, on the other hand, showed that hypothyroidism was seen in 3 boys and 4 girls, of whom 2 were hashimoto, and hyperthyroid was observed in 3 girls and 1 boy.

In another study in 2016, Alves C et al. examined 71 patients with type-1 diabetes. They showed that the mean age of patients was  $11.6 \pm 5.1$ , and the prevalence of thyroid disease was 11.8%, while the prevalence of celiac disease was 7.4% (19).

Considering the increasing prevalence of type 1 diabetes and asthma in children and based on the evidence of the effect of the likelihood of occurrence, exacerbation and course of children's physical disorders, the present study evaluated the prevalence of type-1 diabetes in children. In this cross-sectional study, 3 cases of nasal congestion and 3 cases of allergic rhinitis were observed.

The relationship between celiac disease and type-1 diabetes has also been investigated in several studies (20). Diagnostic and therapeutic errors may occur if accompanied by celiac disease and diabetes and the diagnosis of celiac disease. In our study, the prevalence of celiac disease in type-1 diabetic patients has been investigated, so that the diagnosis of celiac disease in diabetic patients can prevent the progression of this disease and its complications.

In a study conducted by Kylökäs et al., 1358 patients were examined. They showed that 8% of men and 1.8% of women were simultaneously suffering from celiac disease and type-1 diabetes (21). In another study conducted Al-Hakami, the autoimmune disorders were examined in 202 patients with type-1 diabetes. The findings showed that 21 (10.4%) patients experienced celiac disease, while 33 of them (16.3%) had an autoimmune thyroid disease (22). Based on the results of an overview of celiac disease in Iran, this disease was estimated to range from 3.4 to 6.8% (23). In this study, celiac disease was observed in 11.3% of the cases. Accordingly, the prevalence of celiac disease was reported to be: 6.8% by Ghergherehchi(24), 3.4% by Moayeri (25), and 6.25% by Fallahi(24). Another study in Egypt (25)

cited this outbreak to be 6.4%, which is consistent with and very similar to that of Iranian studies. Similar to these results, a study by Aarabi and Chaimarr examined the prevalence of celiac disease in 119 patients with type-1 diabetes. Their findings showed that 5% of children, who were all boys, had anti-TTGs, and the prevalence of proven celiac disease was found to be 4.2% by biopsy (26).

### **5. Conclusion**

In the present study, the prevalence of type-1 diabetes in children of Mazandaran province was documented to be 0.04% and 4.8 per 100,000. This study showed that type-1 diabetes was more prevalent in Mazandaran province than other areas in southern Iran as well as neighboring countries such as Russia and Kuwait. Unfortunately, only 2 studies have been conducted in this regard in Iran. Considering the ethnic and cultural differences in different provinces of the country, it is necessary to conduct such studies in other parts of the country, as well. It was found that the early diagnosis of diabetes prevents unwanted and irreversible diabetes. Due to the fact that the prevalence of type-1 diabetes has been higher in northern Iran than in neighboring countries, this disease should be focused on more and be in the center of doctors' attention.

### **Limitation**

Having access to all information was a difficult and time-consuming process, and in some cases, it took a long period of administrative procedures. This study was conducted on patients aged 6 months to 18 years, so the results may not be generalized to adults.

### Acknowledgements

The authors would like to appreciate health insurance organizations, and doctors of endocrine diseases, as well as rural and urban health centers of the province, Mazandaran Health Insurance, Social Security Organization, Armed Forces Insurance, and Imam Khomeini Relief Committee.

### Conflicts of interest

Authors declare no conflict of interest.

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