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# Incidence of Type 1 Diabetes Mellitus in Hamadan West Region of Iran-2019 - 2020

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## Abstract

**Objective:** Type 1 diabetes mellitus (T1DM) results from the autoimmune destruction of insulin-producing beta cells of the pancreas. The objective of the present study was to describe the one year (2019-2020) incidence of T1DM in Hamadan west region of Iran.

**Materials and Methods:** All 25 new patients with T1DM resident of Hamadan and its suburbs registered in Besat Hospital, Hamadan, Iran, from March 2019 to 2020 were prospectively reviewed. Information including age, sex, place of residence (urban or rural), season of diagnosis and season of birth were taken from parents through face-to-face interviews.

**Results:** During 1 year survey, a total of 57 cases of newly diagnosed T1DM were identified in our center. Among these, 25 patients were residents of Hamadan city and suburbs. Based on this15 per 100 000 per year new cases T1DM occurred in the resident population of Hamadan areas, higher in boys than in girls (18 vs. 11 per 100 000).The mean age of diagnosis was 8.03 yr. The peak incidence was observed at the age group of 10-14 years. 92% were urban .Most cases were diagnosed in the autumn (44%). 52% had a history of neonatal jaundice and 16% had stressful life events in the family before the onset of diabetes.

**Conclusion:** Our study showed a relatively high incidence of T1DM according category of the WHO, being greater in boys and in the age group of 10 to 14 years. The incidence is lower than in some Middle Eastern countries.

**Keywords**: Characteristics, Incidence, Diabetes mellitus, Type 1

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## Introduction

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease in which a combination of genetic predisposition, immune dysregulation and exposure to environmental triggers leads to selective destruction of pancreatic β cells, absolute insulin deficiency and the need for lifelong exogenous insulin therapy (1,2).

Type 1 diabetes is the most common form of diabetes in children with a steadily increasing global incidence of about 3 to 5% per year over the past two decades (3-6) .The main reasons for the increased incidence of T1D are unknown, but may be due to changes in the environment and lifestyle (7).

A large number of epidemiological researches on the global spread T1DM have revealed significant variability in age, sex, seasonality, prevalenceamong ethnicities and geographic areas (8-10). The incidence of T1DM varies from 0.1 per 100,000 per year in parts of Venezuela and China to 40.9 per 100,000 in Finland (8). However, for most of the world's population, accurate data on the epidemiology and possible triggers of type 1 diabetes is still lacking (11). Global heterogeneity in the development of type 1 diabetes may be due to different non-genetic risk factors that are important in the pathogenesis and initiation of the autoimmune process.

Epidemiological studies play an important role in investigating risk factors, potential triggers, strategies for prevention, and treatment of T1DM.To the best of our knowledge, there is no published on incidence of T1DM in our region.

The objective of the present study was to describe the one year (2019-2020) incidence of T1DM in Hamadan west region of Iran.

## Material and methods

The study population included all children under the age of 18 who were at risk of T1DM in Hamadan during one year of study. A retrospective study was conducted on new cases of T1DM during a calendar year from March 21, 2019 – March 21, 2020. All newly diagnosed cases of T1DM aged less than 18 less years of age living in the region of Hamadan for at least 1year prior to diagnosis were studied prospectively by census details.

The pediatric and adolescent endocrinology outpatient clinic of Besat Hospital in Hamadan is the center where all new cases of T1DM are registered. Hamadan is a relatively large, cold and mountainous city in west of Iran among Middle East country.

Research data from all participants were taken from parents through face-to-face interviews. The primary outcome measure was incidence of T1DM per 100 000 person per 1 year in Hamadan city and its suburbs. Secondary objectives included age, sex, place of living (urban, rural), birth weight, birth order, birth seasonality, season of presentation, infant feeding, mean mother age at pregnancy, neonatal jaundice, family history of type 1 diabetes and stressful life events (parental death, drug abuse, conflicts, unemployment and divorce) experienced in the years preceding the onset of diabetes.

The samples were divided into four age groups: 0-4, 5-9, 10-14and 15-18 years.

T1DM was doctor diagnosed based on the presence of classic symptoms of hyperglycemia (thirst, polydipsia, polyuria), weight loss, a random plasma glucose ≥200 mg/dL and fasting glucose level ≥126 mg/dL at diagnosis plus daily insulin injections requirement (12-14).

The one-year incidence rates were calculated by dividing the newly diagnosed cases of T1DM in children and adolescents aged less than 18 years by population at risk aged under 18 years living in Hamadan in the same year and expressed per 100,000 people per year.

Inclusion criteria were all children and adolescents < 18 years of age newly diagnosed T1DM living in Hamadan and its suburbs. The exclusion criteria was parental non-agreement to participate in the study.




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Based on the following criteria the incidence was classified into five groups (15):

- Very low :< 1/100,000 per year
- Low: 1-4.99/100,000 per year
- Intermediate: 5-9.99/100,000 per year
- High 10-19.99/100,000 per year
- Very high ≥20/100,000 per year

### Statistical analysis

Data were analyzed using SPSS -16. The mean and standard deviation were used to express the of participants' quantitative characteristics. The frequency and percentage were used for qualitative characteristics. The incidence of the T1DM was estimated based on the number of new cases and the population at risk at the beginning of the study.

## Ethical considerations

The study protocol was approved by the Ethics Committee of Hamadan University of Medical Sciences (No: IR.UMSHA.REC. 1398.152.) informed written consent was obtained from parents for recruitment prior to participating in the study.

## Results

A total of 57 newly diagnosed patients of Hamadan province were registered as having T1DM. Of these, about half of them (25 patients) living in the city of Hamadan and its suburbs. Based on this, the number of new cases of T1DM for subjects under 18 was estimated at 15 per 100 000 per year. Girls had an incidence of 11 per 100,000 whereas boys had an incidence of 18 per 100,000. (male/ female ratio 1.7). The means age at diagnosis was 8.03 years (range 1.5 -16.5) years. The incidence was higher in boys (% 64) and in the age group of 10 to 14 years (%36). %92 percent were urban residents. Mean mother age at pregnancy was 26.23 ±5.6 years. Mean birth weight was 3.18kg. Sixty-four percent of cases were the first child in the family. Onset of the disease was higher in autumn (44%). Most patients (36%) were born in summer. Fifty-two percent of the studied subjects had a history of infant jaundice and 20% of them had stressful events before the onset of diabetes. About 4% had a sibling with T1DM. Demographics and Characteristics of the subjects with newly T1DM of are shown in Table 1.

## Discussion

The incidence rate of T1DM in children and adolescents living in Hamadan was 15 per 100,000 people, making it one of the countries with the "high" incidence area category of the WHO project classification for diabetes (15,16). There was no significant relationship between the season of birth and the incidence of diabetes Our findings on the incidence of T1DM in children are similar to those of a meta-analysis of 193 articles from 1990 to 2019 around the world (15 per 100 000) (17). The incidence is lower than Finland and other Scandinavian countries (36.8 and 36.5 / 100 000 / year, respectively) and higher than China and Venezuela (1.01 and 0.1/100 000, respectively) (15,18,19).

The incidence of the T1DM in our region is lower than the prevalence reported in some Middle Eastern countries such as Saudi Arabia. (27.3-33. 5 per 100,000 individuals / per year (20,21), Kuwait (44.5/ 100 000 (22), Qatar 33.2 /100,000 (23) and higher than those reported s in Pakistan (1/100 000) (24) and Korea (4.45 100 000) (11). Among the Middle East, there is a significant variation in the incidence of diabetes. Qatar and Kuwait have the highest rates and Oman and Jordan have the lowest rate (25,26). This obvious difference can be attributed to genetics or climate as well as the influence of various environmental factors. Epidemiological data from 100 different populations around the world also show a wide (more than 350 times) geographical difference in the incidence of type 1 diabetes (0.1 to 57.6 per 100 000) (15,22). The differences in incidence between countries might be partly due to genetic differences. However, the differences within countries and large differences between neighboring countries with similar genetic composition can be attributed to putative and

**Table1. Demographic characteristics and some environmental factors in newly diagnosed T1DM (n=25)**

| Characteristics | Results |
|---|---|
| **Age distribution at diagnosis (yr), n (%)** | |
| 0-4 | 7 (28) |
| 5-9 | 8 (32) |
| 10-14 | 9 (36) |
| 15-18 | 1 (4) |
| **Gender, n (%)** | |
| Male | 16 (64) |
| Female | 9 (36) |
| **Living location, n (%)** | |
| Urban | 23 (92) |
| Rural | 2 (8) |
| **Mother's age at delivery (yr), mean (SD)** | 26.23± (Range 17-36) |
| **Birth Weight (gr)** | 3182.6±435.5 |
| **Birth order, n (%)** | |
| First Child | 16 (64) |
| Second Child | 8 (32) |
| Third child | 1 (4) |
| **Season of onset, n (%)** | |
| Spring | 5 (20) |
| Summer | 6 (24) |
| Autumn | 11 (44) |
| Winter | 3 (12) |
| **Season of birth, n (%)** | |
| Spring | 5 (20) |
| Summer | 9 (36) |
| Autumn | 7 (28) |
| Winter | 4 (16) |
| **Feeding during the first 6 months of life** | |
| Exclusively breastfeed | 18 (27) |
| Formula | 5 (20) |
| Mix | 2 (8) |
| **Neonatal jaundice, n (%)** | 13 (52) |
| **First degree relatives with T1DM, n (%)** | 1 (4) |
| **Stressful Events n (%)** | 5 (20) |
| **Parental Consanguinity, n (%)** | |
| No | 23 (92) |
| Yes | 2 (8) |
| **Father's education, n (%)** | |
| Illiterate | 0 (0) |
| Elementary | 8 (32) |
| Diploma | 6 (24) |
| Academic | 11 (44) |
| **Mother's education, n (%)** | |
| Illiterate | 1 (4) |
| Elementary | 8 (32) |
| Diploma | 11 (44) |
| Academic | 5 (20) |

possible unknown environmental triggers that initiate the autoimmune process of T1DM (2).

Putative triggers include geographical and climatic conditions, residence, socio-economics, nutrition, infections, family environment, psychosocial stress, vaccines, toxic agents, air pollution, hygiene hypothesis, intestinal microbiota, lack of vitamin D as well as other putative environmental risk (2,10,25,27). Accordingly, more efforts are needed to identify environmental factors and their effect on predisposing or protective genes for T1DM in the general population.

In confirmation of previous studies, the mean age of diagnosis was 8.3 yr (26,28). The incidence of T1DM was higher in the age group of 10 to 14 years and lower in




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adolescents over 15 years which was similar to those found in other studies (2,21,29,30).

Similar to the results of some previous studies, Our data show that the incidence of type 1 diabetes was higher in boys than girls (2,31,32). The overall sex ratio for type 1 diabetes in children is about equal, however, some studies show that T1DM may be slightly more common in boys than girls (2,10,21,33-35). Overall, it is not possible to make a definitive statement about the gender differences in T1DM.

According with previous studies (36-39), we noted a significant predominance in the incidence of diabetes in urban child compared to rural ones. This finding was expected because a high percentage of patients live in the city and the urban population is more than the rural population**.**

Contrary to the results of some previous studies, we found that the onset of T1DM was more in autumn and summer, respectively, which was a different seasonal pattern. In our previous study, most cases of T1DM were diagnosed in summer and spring, which was a different pattern (14,40). Epidemiological studies in other parts of world indicated that most children with T1DM are diagnosed in the winter (16,21,32,41-47)**.** This finding may indicate that different triggers cause T1DM in our region.The pattern of infectious diseases, exposure to sunlight and its effects on vitamin D levels that have beneficial effects against the development of T1D, different diets and exercise can also explain the seasonality of T1DM (48-50). Consistent with the opinion of previous researchers, we hypothesize that the different seasonal pattern of T1DM in this study is due to the different environmental factors includes geographic location, lifestyle, viral infectious epidemic and air pollution that trigger immune system (3,11). Different pattern of T1DM onset with a predominance in spring has also been reported in southeastern Turkey and Japan (28,51). In contrast to our findings, the results of a previous cohort study in Japan by Kida et al. did not show seasonal differences in the onset of T2DM (52). Regarding the birth seasonality, current study showed that most of the patients were born in summer and autumn. There was no significant relationship between the season of birth and the incidence of diabetes. In confirmation of our results, Við Streym et al. stated that the season of birth has no significant effect on development of T1DM (53). A study from Ukraine reported a strong seasonal birth pattern with the lowest rates of T1D in fall and the highest in spring (54). Similar reports of higher rates of T1D among youth born in spring and lower rates among youth born in the autumn or winter have been published from Europe (9,48). The effect of the birth season on the subsequent incidence of type 1 diabetes has been linked to maternal vitamin D deficiency and exposure to environmental pathogens in the uterus or perinatal period (48,55,56).

The occurrence of T1DM is strongly influenced by genetic predisposition and people who have first-degree relatives are more susceptible with T1DM than the general population (9). However, the results of various studies indicated that most cases of T1DM occur sporadically rather than familial. In this regard, the data of the current study also showed that only 4% of patients had a first-degree relative with T1DM.

The present study founds also that about half of patients had a history of neonatal jaundice requiring phototherapy. There is a dearth of evidence regarding the association between jaundice and T1DM. Our finding is in accordance with the results stated by some previous studies (57-61), but was inconsistent with the finding of studies conducted by Newman et al, Robertson L et al and Waernbaum et al. which reported no association between increased risk of T1DM in children and history of neonatal jaundice or phototherapy (62-64). It is not clear how jaundice contributes to diabetes. It may be assumed that jaundice is a symptom of an underlying disease that accelerates the destruction of beta cells. This association needs further exploration (65).




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In this study, 20% of subjects had stressful events in the family before the onset of diabetes. In our previous research, we showed that children with diabetes experienced major stress such as family breakup and parental addiction with a significant frequency compared to the control group before the onset of the disease (66). The impact of psychological stress as a trigger or accelerator of type 1 diabetes has been widely studied in the literature, but the findings have often been contradictory (67-69). This research contributes to our understanding of the potential role of psychological stress in childhood as one of the environmental triggers.

Limitations: We acknowledge several limitations to our work: first, this work is a one -year prospective study and dealing with single center and single region of the country and therefore its results may not be representative of a larger population and generalizable to the country of Iran. Second, some new case of T1DM may have not been included in the analysis for various reasons including referring to medical centers in other cities or starting outpatient treatment. Despite these limitations, we believe that the inclusion and exclusion criteria in the present study were as complete and practical as possible and included almost all new T1DM. Therefore, we reported a relatively accurate incidence of T1D in our region.

## Conclusions

The incidence of T1DM in children under 18 years was 15/100,000 during 2019-2020 in the Hamadan west region of Iran, being greater in boys and in the age group of 10 to 14 years. Presentation of T1DM in our region exhibits a distinct seasonal pattern. This study is the first on local incidence and environmental patterns of T1DM in children under 18 years in Hamadan, Iran in 2020.

The results of this study can be a basis for more comprehensive epidemiological studies in the future about the prevalence and incidence of type 1 diabetes in different regions of Iran. This descriptive study also clarifies some environmental factors before T1DM. Identifying the environmental factors that trigger diabetes can lead to encouragement to provide preventive and therapeutic strategies in this area.

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## Conflict of Interest

Authors have no conflicts of interest

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