DOI: 10.14744/iksstd.2022.60024
İKSSTD 2022;14(2):180-185

ORIGINAL INVESTIGATION / ÖZGÜN ARAŞTIRMA

Is the Season of Diagnosis Changing in Children with Type 1 Diabetes Mellitus?

Tip 1 Diabetes Mellitus Hastalarında Tanı Mevsimi Değişiyor mu?

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ABSTRACT

Objective: By the effect of global warming, climate model of Turkey is suggested to evolve through semi-arid seasons and to the tropical climate. This study aimed to determine the seasonability for clinical onset of Type 1 diabetes mellitus (T1DM).

Method: T1DM patients newly diagnosed between 2014 and 2019 in our pediatric endocrinology department located in Istanbul were included in this study. Clinical onset date and age of diagnosis of diabetes were recorded for each patient. Using the worldwheatheronline.com website, regional average rainy days, cloudy days, sunny days, temperature, and ultraviolet index (UVI) were calculated per month for the past 6 years.

Results: A total of 659 patients with the new onset T1DM included in this study. A number of new diagnosed patients were 29.1% (192) in winter, 22.8% (150) in spring, 17.6% (116) in summer, and 30.5% (201) in autumn, respectively. No significant effect of the rainy day, cloudy day, sunny day, temperature, and UVI average of the month of diagnosis could be detected on this seasonal shift. Similar results were obtained when 132 patients whose under 4 years of age at the time of diagnosis were excluded from the study data.

Conclusion: Although weather conditions seemed to have no considerable effect on this seasonal shift, the T1DM onset in the autumn season was seen to be shifted to the spring season, partially. Further studies including large number of participants are needed for a better understanding of the seasonality of T1DM worldwide.

Keywords: Children, seasonality, Type 1 diabetes mellitus, ultraviolet index

ÖZ

Amaç: Küresel ısınma ile birlikte Türkiye'de mevsimlerin yarı kurak ve tropik iklim özelliklerine doğru evrildiği, son yıllarda sonbahar ve ilkbahar hava koşullarının yarısının kışa, yarısının da yaza benzer seyrettiği düşünülmektedir. Bu çalışmada, tip 1 diabetes mellitus klinik tanı zamanında mevsim değişikliğinin ve bu duruma hava koşullarının olası etkisinin incelenmesi amaçlandı.

Yöntem: Çalışmaya İstanbul'daki çocuk endokrinoloji kliniğimizde 2014 ile 2019 yılları arasında yeni tanı almış 18 yaş altı tip 1 diabetes mellitus hastaları dahil edildi. Her hasta için klinik belirti başlangıç tarihi ve diyabet tanı mevsimi ile demografik veriler kaydedildi. Worldwheatheronline.com web sitesi kullanılarak İstanbul ilinin son beş yılındaki tip 1 diabetes mellitus tanı ayına ait aylık ortalama yağışlı gün, bulutlu gün, güneşli gün sayısı, sıcaklık ve ultraviyole indeks ortalaması saptandı. Hastaların tanı yaşı ile tanı mevsimi ve hava koşulları arasındaki ilişki istatistiksel olarak değerlendirildi.

Bulgular: Çalışmaya 659 yeni tanı almış tip 1 diabetes mellitus hastası alındı. Çalışmaya alınan hastaların %50,4'ü kız (n=332), %49,6'sı (n=327) erkek idi. Mevsimlere göre yeni tanı konulan hasta sayısı sırasıyla kışın %29,1 (n=192), ilkbaharda %22,8 (n=150), yazın %17,6 (n=116) ve sonbaharda %30,5 (n=201) idi. Çalışma süresince tip 1 diabetes mellitus klinik başlangıcının kış ve sonbahar aylarında yüksek ilkbahar ve yaz aylarında düşük olduğu görülmekle beraber istatistiksel anlamı olacak şekilde 2016 yılı ve sonrasında sonbahar mevsimindeki diyabet başlangıç ağırlığının bir kısmının ilkbahar mevsimine

Cite as: Önal H, Yılmaz Semerci S, Topuz HŞ, Adal SE. Is the Season of Diagnosis Changing in Children with Type 1 Diabetes Mellitus? İKSSTD 2022;14(2):180-185

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Received/Geliş tarihi: 19.07.2021
Accepted/Kabul tarihi: 18.04.2022

kaymış olduğu izlendi. Ancak mevsimsel bu kayma üzerinde tanı ayına ait yağışlı gün, bulutlu gün, güneşli gün, sıcaklık ve ultraviyole indeks ortalamasının anlamlı bir etkisi saptanmadı. Tanı sırasında dört yaşın altında olan 132 hasta çalışma verilerinden çıkarılarak yapılan istatistiksel değerlendirmede sonuçların değişmediği görüldü.

Sonuç: Çalışmamız ile sonbahar mevsimindeki diyabet başlangıç ağırlığının bir kısmının ilkbahar mevsimine kaymış olduğu tespit edilmiş olup bu mevsimsel kaymaya hava koşullarının etkisinin olmadığı görüldü. T1DM tanısında mevsimsel özelliklerin etkisini daha iyi değerlendirebilmek için daha çok sayıda hasta içeren geniş kapsamlı çalışmalara gereksinim duyulmaktadır.

Anahtar kelimeler: Çocuk, mevsim, Tip 1 diabetes mellitus, ultraviyole indeks

INTRODUCTION

Affecting 23.6–65/100.000 children under the age of 15 worldwide, Type 1 diabetes mellitus (T1DM) is still one of the most common chronic diseases in children.[1,2] Although it is believed that environmental factors such as viral infections activate the immune system to harm beta cells which result in insulin deficiency in genetically predispozed persons, exact pathogenesis of T1DM remains unclear even today.[1,3] Epidemiologic data are crucial for a better understanding of the underlying mechanisms that trigger or cause T1DM. The clinical onset of T1DM is known to be mostly in winter and autumn instead that the incidence of T1DM was recorded lower in summer and spring.[2–5] T1DM peaks are seen in autumn and spring. It is also more common in countries with low sun exposure, such as Finland.[3] The relationship between diabetes and seasons has been known for a long time and it has been explained by factors such as less sunless Vitamin D, seasonal virus density (the triggering effect of increasing viral infection frequency in certain seasons).[4] It has been suggested that T1DM peaks develop after rainy months.[2] Depending on this data, we hypothesize that there is a possible relationship between the change in the diagnosis months of diabetes and the change in seasonal characteristics (global warming effect) in recent years. Therefore, the present study aimed to determine the season for clinical onset of T1DM patients who were newly diagnosed between 2014 and 2019 in our clinic located in Istanbul, and to examine the change of seasonal relationship over the years and the effect of weather conditions on this change.

METHOD

A total of 659 T1DM patients newly diagnosed between 2014 and 2019 in our clinic located in Istanbul were included in our study. Local Ethics Committee of Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital approved the study (Ethics Committee approval number: 2020-79). Clinical onset date and age of diagnosis were recorded for each patient. Using the worldwheatheronline.com website, the monthly average rainy days, cloudy days, sunny days, temperature (degree in Celcius), and ultraviolet index (UVI) for the past 5 years in Istanbul province were calculated.[6] UVI scale which is established by the World Health Organization is used in this study.[7] Local Ethics Committee approved the study (Ethics Committee approval number: 2020-79). All participants were included the study following their approval of written informed consent.

Statistical Analysis

Comparisons of groups were performed by MANOVA. IBM SPSS Statistics for Macintosh, Version 26.0 (Armonk, NY: IBM Corp) was used for statistical analysis. Variance homogeneity was tested for each dependent variable with Levene's test. Covariance values between groups were compared using Box's test. Statistical significance was accepted when the probability $p<0.05$ and changes were referred to as significant at this p value.

RESULTS

The number of T1DM patients newly diagnosed in our clinic between 2014 and 2019 was 659. The mean age of our patients was 9.5 years (min–max; 1–17.96). The gender distribution was recorded as 50.4% female and 49.4% male, respectively. A number of new diagnosed patients were 29.1% (192) in winter and 22.8% (150) in spring. Clinical onset of T1DM was more frequent in the winter and autumn than the spring and the summer; but from the beginning of 2016, it was observed that a considerable part of the T1DM onset in the autumn season shifted to the spring season ($p=0.06$), (Table 1 and Fig. 1).

Comparing the monthly rainy days, sunny days, cloudy days, and monthly average temperature levels for the seasons between 2014 and 2019, no significant difference was found in terms of seasonal weather conditions by years (Table 2 and Fig. 2). Likewise, the seasons have not changed in terms of UVI over the years. Since a seasonal pattern was not reported in children younger than 4 years, 132 patients below 4 years of age were excluded from the study data and then the group

Table 1. Seasonal change of the month of diagnosis by years in T1DM patients

Year	Winter		Spring		Summer		Autumn		Total
	n	%	n	%	n	%	n	%	
2014	26	25.5	17	16.7	15	14.7	44	43.1	102
2015	40	29.4	26	19.1	20	14.7	50	36.8	136
2016	34	27.2	31	24.8	28	22.4	32	25.6	125
2017	26.6	29	30.3	33	19.3	21	23.9	26	109
2018	34	34	23	23	16	16	27	27	100
2019	33.3	29	23	20	18.4	16	25.3	22	87
Total									659

T1DM: Type 1 Diabetes mellitus; n represents the number of patients who had a first diagnosis of T1DM per month

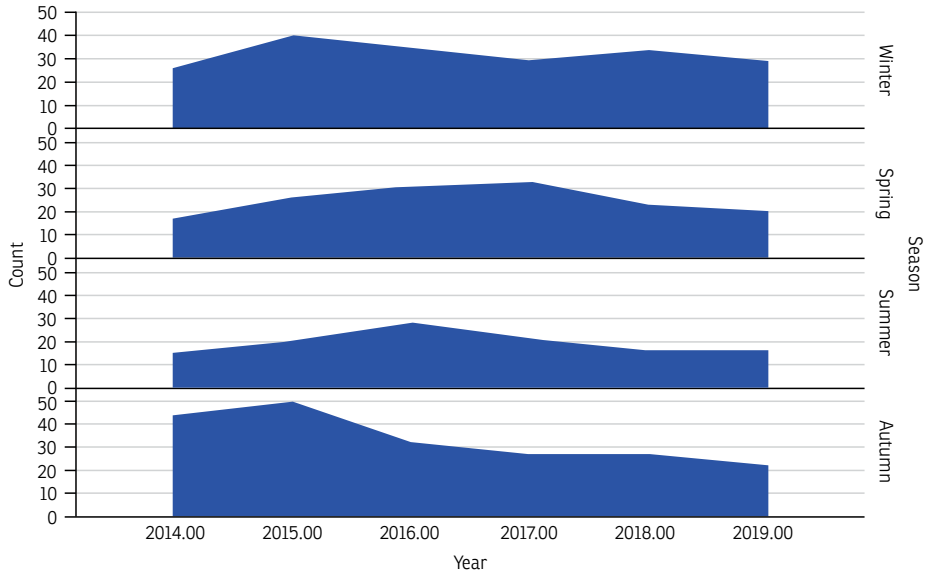

Figure 1. Seasonal change of the number of patients who were newly diagnosed as T1DM by years

T1DM: Type 1 Diabetes mellitus

comparisons were repeated with 537 patients, it was observed that the statistical results did not change. It has been observed that the UVI in Istanbul province is always below 3 during the winter months (Fig. 3). Since the p-value obtained from the Box's test result was higher than 0.05, there was an equality of covariance between the groups. Variances of dependent variables were homogeneous in Lewene test. In the Wilks'Lambda test, p value was found 0.198, Partial Eta Squared 0.086.

DISCUSSION

The present study demonstrated the seasonal variability of T1DM diagnosis between the children followed up by a relatively large hospital in Istanbul. The effect of this variable seasonal pattern is explained by the role of infections and the lack of sunlight exposure in the literature.[8,9] Considering the higher incidence of infections, especially virus caused ones in winter, it is not that surprising to see more patients of new onset T1DM in this season. Besides, reduced endogeneous Vitamin D production due to the inadequate sunlight exposure may contribute to the abnormal immune modulation in T1DM.[9] Nevertheless, the time elapsed between the event of the trigger and the onset of hyperglycemia is hard to predict and the effect of the climate on this process is still not clarified well.

Table 2. Comparison of the weather conditions of the seasons depending on the years (2014–2019)

Years 2014–19	p	Winter	Spring	Summer	Autumn
Rainy day		0.35	0.56	0.66	0.73
Sunny day		0.06	0.86	0.86	0.13
Cloudy day		0.34	0.62	0.25	0.20
Temperature		0.93	0.40	0.40	0.98
UV index		0.26	0.70	0.79	0.73

MANOVA test

The seasonal variability is associated with the infectious triggers and inadequate sun exposure in the pathogenesis.[8,9] The putative infectious agents, notably viruses, are more frequent and long-lived in winter. Given their involvement in the pathogenesis, the number of new cases should be higher in winter. In addition, the reduced number of sunny days in the winter causes a decrease in the subcutaneous production of Vitamin D that has a significant role in immune modulation.[9] However, the seasonal variability may not be always obvious because of the time elapsed between the intervention of the trigger and the onset of disease is variable.

A seasonal association between the viral infectious agents including Rotavirus, Norovirus, or Enterovirus, and the specific diseases like gastroenteritis, which peak in winter, or hand, foot, mouth disease, that increase in summer, is well-described.[10,11] The impact of ambient temperature is thought to be inevitable on the survival or infectivity of microbial agents. Recent studies pointed that hand, foot, and mouth disease caused by Enteroviruses could lead to the diagnosis of T1DM within a month.[12] Besides, the current data demonstrated that blood glucose levels were detected to be in a higher range in colder seasons.[13] Therefore, this may result in an elevated need of insulin which could be contributive in the onset of T1DM. Furthermore, elevations of insulin levels by non-specific viral infections may fasten the process of T1DM to be clinically apparent.[14]

Ambient temperature has been related with seasonality in particular infections such as winter peaks in gastroenteritis due to the eased survival at low temperature of Rotavirus and Norovirus.[10] Furthermore, Enteroviruses can be the reason for hand, foot, and mouth disease, which is most common in summer.[11]

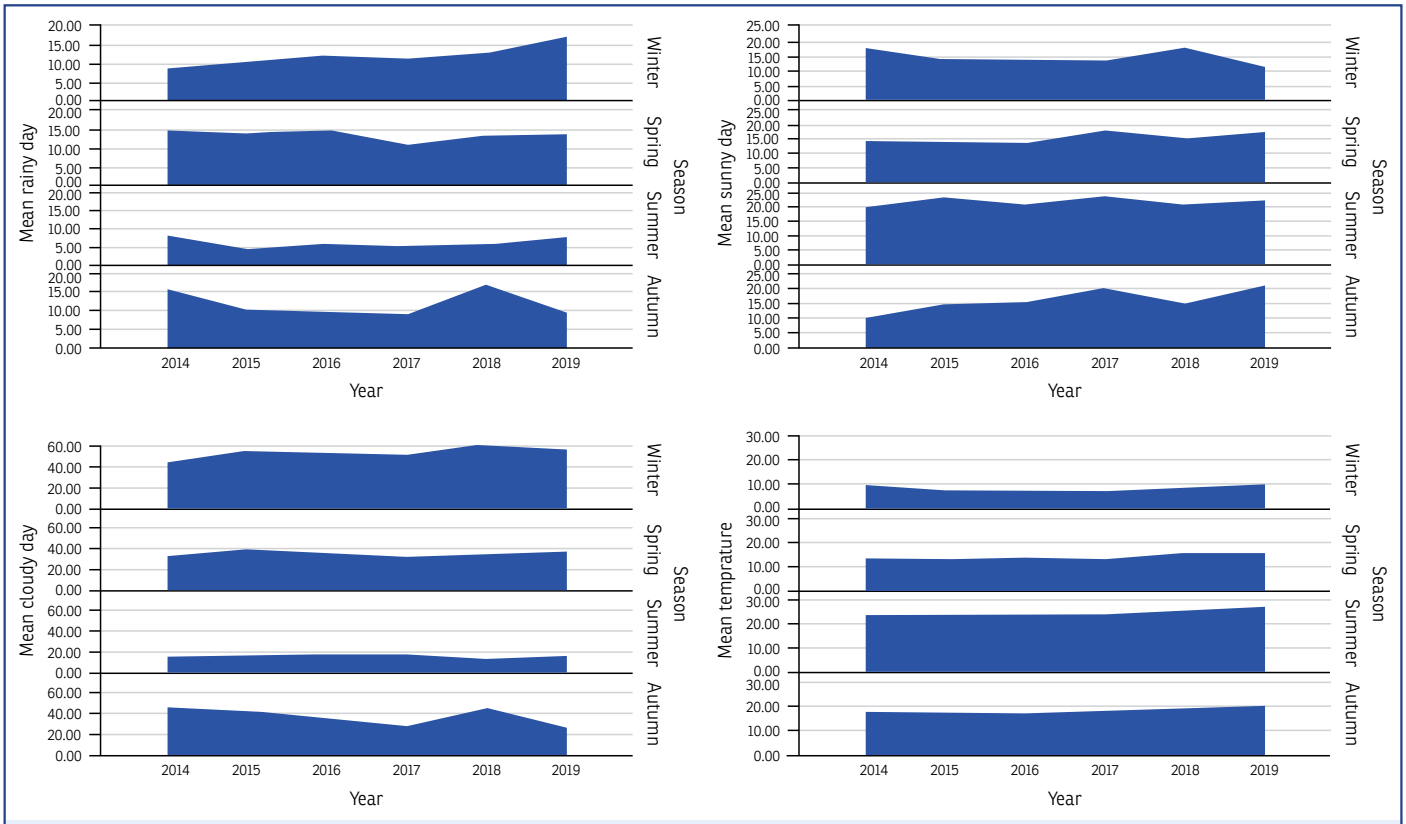

Figure 2. Comparison of rainy days, sunny days, cloudy days, and average temperature according to the seasons between 2014 and 2019

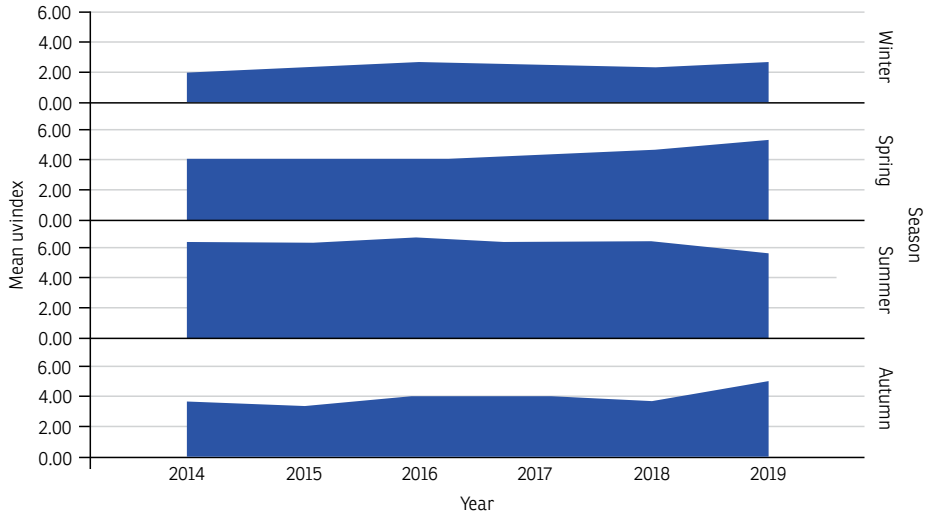

Figure 3. Seasonal change of ultra violet index by years

Enteroviral infections were reported to be markedly increased within a month of T1DM diagnosis.[12] In addition, scientific evidence points that blood glucose is measured higher in colder months than others[13] and may thus precipitate disease onset because of an increased insulin requirement. Non-specific viral infections may also curtail the time elapsed before T1DM becomes clinically apparent by increasing insulin demand.[14]

While the significance of season variability is more evident in children aged 10–14 years, it was not that obvious in those aged 5–9 years. It is another topic worth to investigate that there is no seasonality in children aged 0–4 years.[15] This may be associated with the lower infection incidence in this age group due to the lack of admission to communities before 3 years. Furthermore, the possible regional pattern of seasonality may need to be elucidated. For example, it should be enlightened why Japanese children, aged 0–14 years, did not follow a seasonal variability of T1DM for the years 1983–1992.[16]

Seasonality of T1DM was more evident in children aged 10–14 years, although this was less clear than in those aged 5–9 years. Some characteristics of the countries, through decreasing exposure to infections, can be explanatory for the quite stable prevalence of TIDM of ages 0–4: Children are raised by their parents in the first 2 years of life (this is the length of the parental leave), by their grandparents in the following year. Participating to communities, where infections are more frequent, generally occurs behind 3 years of age. However, such seasonality is not universal as no seasonal pattern was found in Japanese children aged between 0 and 14 years nor in the Baltic states.[15,16]

Vitamin D synthesis is only possible with a UV index of 3 and above.[17] In our study, the UV index was below 3 in the winter months in Istanbul. By the effect of global warming, climate of Turkey is suggested to evolve through semi-arid seasons and to the tropical climate. As a result of this, in recent years, one half of autumn and spring was believed to be felt like winter, besides the other part was more like summer. In accordance with the literature, in our study period of those 6 years; the clinical onset of T1DM was higher in the winter and autumn months than the spring and the summer. However, statistically significantly, beginning with the year of 2016, it was observed that some of the diabetes onset weight in the autumn season shifted to the spring season. However, no significant effect of the rainy day, cloudy day, sunny day, temperature, and UVI average of the month of diagnosis could be detected on this seasonal shift. There may be two explanations for this: First one is that the weather parameters that we have chosen are not sufficient to show seasonal shift. Second one may be the shift in the season of diagnosis that could depend on external factors such as migration events or changes in admissions from other centers.

Study Limitations

There were also some limitations of the present study due to the design and restricted time interval. First, since this study was conducted in a retrospective design, data had some lack. Furthermore, the number of the participants was another restriction. Although Istanbul is a good sample as a metropolitan with lots of non-native born residents, without involving participants of other large cities from the various geographic regions, it cannot reflect the whole country.

CONCLUSION

It was found that the T1DM onset in the autumn season shifted somewhat to the spring season. However, weather conditions seemed to have no effect on this seasonal shift. To clarify the situation of our country, further studies are required in a larger patient group of new onset T1DM in different regions, for a wider time interval.

Disclosures

Ethics Committee Approval: The study was approved by the Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (No: 2020-79, Date: 11/11/2020).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

Authorship Contributions: Concept: H.Ö., S.Y.S., H.Ş.T., S.E.A.; Design: H.Ö., S.Y.S.; Supervision: H.Ö., S.Y.S., H.Ş.T., S.E.A.; Funding: H.Ö., S.Y.S., H.Ş.T., S.E.A.; Materials: H.Ö., H.Ş.T., S.Y.S.; Data Collection or Processing: H.Ö., S.Y.S., H.Ş.T., S.E.A.; Analysis or Interpretation: H.Ö., H.Ş.T.; Literature Search: H.Ö., S.Y.S., H.Ş.T., S.E.A.; Writing: H.Ö., S.Y.S.; Critical review: H.Ö., S.Y.S., H.Ş.T., S.E.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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