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Evaluation of children with type 1 diabetes in Kırıkkale

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ABSTRACT

Aims: The aim of this study is to evaluate the clinical laboratory and demographic characteristics of children aged 0-18 with Type 1 Diabetes who applied to Kırıkkale University Hospital,

Methods: Patients who applied to Kırıkkale University Medical Faculty Hospital between January 2011 and January 2021 and were diagnosed with Type 1 diabetes mellitus were included in the study. From file information; age at admission, age at diagnosis and laboratory values at admission were recorded.

Results: Of the children, 48 (48.5%) were boys and 51 (51.5%) were girls. The mean age of all patients was 14.4±2.1 years. It was observed that its frequency increased during the adolescence period. It appeared that patients frequently increased in the autumn and winter months. Vitamin D was low in 74.4% of the patients. Statistical significance was found between HbA1c of those who applied to the hospital with a diagnosis of diabetic ketoacidosis.

Conclusion: It is instructive to investigate the regional characteristics of the disease in terms of genetic and environmental factors that have an important place in the etiology. The findings of our study were consistent with similar studies and literature.

Keywords: Kırıkkale, type 1 diabetes, child, hemoglobin A1c

INTRODUCTION

Type 1 diabetes mellitus (DM) is the most common chronic disease of childhood and adolescence that results in hyperglycemia due to insulin deficiency that develops due to destruction of pancreatic beta cells due to autoimmunity, viral chemical and toxic reasons. The illness develops in people with genetic predisposition, under the influence of environmental and autoimmune factors. Patients need insulin replacement due to the permanent absence of insulin.[1,2] Compared to previous years, the incidence of new type 1 DM cases detected worldwide in recent years seems to have increased gradually.[3] The basis of diabetes treatment is to provide glucose values close to normal and to increase the quality of life by minimizing the microvascular complications that occur in the future. Chronic complications caused by diabetes lead to more frequent hospital admissions and long-term hospitalizations. As a result, it causes both labor loss and economic losses.[4] Despite the increase in the incidence of type 1 DM worldwide and the changes in admission findings at the time of diagnosis, the data on the incidence of type 1 DM and clinical presentation findings in our country are not sufficient. In this study, it was aimed to evaluate the demographic, clinical and laboratory characteristics of patients aged 0-18 who diagnosed with Type 1 DM, who applied to Kırıkkale University Medical Faculty in the last 10 years, and compare them with the literature findings.

METHODS

The study was approved by the Kırıkkale University Faculty of Medicine Ethics Committee on 08.07.2021 (Decision No: 2021.07.09). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study group was formed retrospectively examining the files of patients who were diagnosed with diabetes at the time of their first admission to the Pediatric Endocrinology and Diabetes Polyclinic, Pediatric Health and Diseases Polyclinics, and Pediatric Emergency Departments in University Hospital between 01.01.2011 and 01.01.2021. Demographic data such as gender, age, season at the time of diagnosis, diabetic ketoacidosis status, and clinical and laboratory information of the patients were recorded in the patient files. Patients with insufficient file data or whose files could not be accessed were excluded from the study.5 As laboratory data, blood glucose, blood gas (pH, HCO3), C-peptide, HbA1c, diabetes autoantibodies at the time of diagnosis were recorded. In the evaluation of metabolic control according to the target recommendations of the

International Society for Pediatric and Adolescent Diabetes (ISPAD) in 2007, if the mean HbA1c is <7.5% good metabolic control, between 7.5-9% moderate metabolic control, and ≥9 % evaluated as poor metabolic control. The subjects were classified into two groups according to the presence of diabetic ketoacidosis aat the time of diagnosis: DKA group and non-DKA groups.

Statistical Analysis

Statistical analysis was performed using the SPPS 21.0 (SPSS Inc., Chicago, IL, USA) program. The homogeneous distribution of the data was evaluated using the Kolmogorov–Smirnov test. Group homogeneity was also examined when comparing the data of two independent groups; student T test was used to compare homogeneously distributed data, and Mann-Whitney U test was used to compare data that did not show homogeneous distribution. All data are presented as median and mean ± SD. Chi-square test was used to compare group ratios. The p value of <0.05 obtained in the comparison of the groups was considered statistically significant.

RESULTS

Of the 99 patients included in the study, 48 (48.5%) were male. The mean age of the patients was 11.56±4.68 years, and the median age was 13 years. The mean age of girls was 11.58±4.68 years, and the mean age of boys was 11.54±4.73 years. Considering the age groups of the patients, we observed peaks between 4-6 years and 10-17 years.

When examining the number of applications by season, we observed that 23 (23.2%) patients applied in spring, 20 (20.2%) in summer, 27 (27.3%) in autumn, and 29 (29.3%) in winter. When the application biochemistry laboratory data of the cases were evaluated, the average biochemical values of all patients are given in **Table 1**.

Table 1. Comparison of the laboratory mean values of the cases

Parameters	n	Median (min-max)
Blood Glucose (mg/dl)	99	295 (81-830)
C-Peptide (ng/ml)	37	0.32 (0-2.67)
HbA1C (%)	99	10.3 (6.5-19.4)
HDL (mg/dl)	99	54 (30-103)
LDL (mg/dl)	99	83 (50-173)
Cholesterol (mg/dl)	99	153 (80-423)
TG (mg/dl)	99	100 (43-618)
Vitamin B12 (pq/mL)	58	373 (36-1667)
Folic Acid (ng/mL)	49	11.4 (2.69-20.0)
Vitamin D (ng/mL)	39	10.2 (3-102)
Insulin auto antibody (U/ml)	38	2.76 (0.01-12.9)

Vitamin D (25OH Vitamin-D) levels were examined in the diagnosis of 39 patients. In the results of these patients, it was observed that the vitamin D level was at least 3ng/ml, maximum 36 ng/ml, and the mean was 13.96±8.45. When patients with vitamin D deficiency (<20 ng/ml) were examined, it was seen that the rate among all patients was 74.4%.

In our study, from the perspective of DKA at the time of application, we observed that 17 (17.2%) patients presented with DKA. When the patients presenting with DKA were analyzed according to gender, it was seen that there was no statistical difference. (p=0.508) The mean age of the patients presenting with DKA was 11.23±4.58 years, while those without DKA were 11.63±4.75 years old (p=0.745). When the patients presenting with DKA were examined in terms of HbA1c at admission, a significant difference was observed. (p<0.005). When the laboratories of the patients were evaluated, there were only differences in blood glucose, blood gas and blood HCO3 between the patients who presented with DKA and those who did not present with DKA (**Table 2**). When the patients presenting with DKA were analyzed according to the season, no statistical difference was found. (p=0.168).

Table 2. Comparison of patients with DKA and Non-DKA

Parameters	DKA	Non-DKA	p
Num. of Applications (%)	17	82	
Gender (boy/girl)	7/10	41/41	0.508
Age (Mean ± STD)	11.23 ± 4.58	11.63 ± 4.75	0.745
HbA1c (%)	11.69 ± 2.50	10.28 ± 2.55	0.041
Blood Glucose (mg/dl)	460.58 ± 157.72	302.90 ± 167.47	0.001
pH	7.23 ± 0.15	7.39 ± 0.14	0.000
HCO3	13.05 ± 9.12	21.54 ± 6.47	0.000

DISCUSSION

Type 1 DM is the most common chronic endocrine and metabolic disease in the pediatric population. It causes disturbances in carbohydrate, fat and protein metabolism caused by various etiological factors and deficiency of insulin hormone released from pancreatic beta cells. It has a multifactorial etiology including genetic, autoimmune and environmental factors. There are differences in the disease's appearance such as age, race, gender, season, geographical region. Type 1 DM is seen equally in boys and girls in the world.[5] These rates have not changed in recent domestic and international studies.6-10 There was no change in these rates in our study.

In a study conducted by Yeşilkaya et al.10 by obtaining the data of 17175 cases diagnosed between January 2011 and December 2013 from the Social Security Institution of the Republic of Turkey (SGK), the age at diagnosis was found to be 10.6±4.[6] years. In our study, the mean age at which the patients were diagnosed was 11.5±4.7 years. It is thought that the incidence of type 1 DM peaks at the age of 5-7 when exposure to infections increases with starting school, and peaks at the age of 10-14 years when it is triggered by the effects of gonadal steroids, growth hormone and emotional stress.[11] In a study by Acar et al.[12], the peak age of the cases was 4-6 (18.1%) and 8-10 (17%). In a study by Cotellessa et al.13, the most common age at diagnosis was 10-14 years (44.2%), followed by 5-9 years (32.9%). In our study, the number of patients between the ages of 12-16 was found to be 46 (46.4%) and the age at which the disease was most common.

Seasonal differences in type 1 DM are often seen in autumn and winter, when exposure to infection increases.[14] Cotellessa et al.[13] In a study conducted by Italy, it was found that 34.25% peaked in the winter months. In a study conducted by Aydoğan et al.[15] in Çanakkale, it was shown that 32.6% were diagnosed in autumn and 30.43% in winter. In our study, 23.2% of the cases were seen in spring, 20.2% in summer, 29.3% in autumn and 27.3% in winter. Studies have

reported that type 1 diabetes patients are diagnosed more often in autumn and winter, and this may be associated with increased viral infections.[16] We also attributed the increase in autumn and winter months to the more dominant sedentary life in those months.

Glycated hemoglobin (HbA1c), which is the gold standard in the diagnosis of DM and monitoring the adequacy of metabolic control and insulin therapy; It occurs by the glycosylation of glucose by non-enzymatic pathways. For this reason, since it is related to blood glucose level and erythrocyte lifespan, its changes in the blood are slow and reflect the blood glucose level of a 2-3 month period.[17] In two previous studies conducted abroad, mean HbA1c at the time of diagnosis was found to be 11.6±2.6% and 10.6±4.4% in patients with type 1 DM.[18,19] In a study conducted by Demir et al.[20] in our country, HbA1c was found to be 10.5±2.6%. In a study conducted by Taşkın et al.21, HbA1c was found to be 10.8±2.91. In our study, the HbA1c of type 1 DM patients at the time of diagnosis was found to be 10.52±2.59% and it was seen as poor metabolic control in accordance with the literature.

C-peptide is a type of beta cell-secreted marker used in the differentiation of endogenous and exogenous insulin in hypoglycemia, which also shows the production capacity of the pancreas. When patients with type 1 DM were examined in terms of C-peptide levels, in a study conducted by Mayer Davis et al.[21] on 1316 patients with type 1 DM, C-peptide level was found to be 0.69±0.6 (ng/ml). In a study conducted by Xin et al.[22] in China, the mean of C-peptide was found to be 0.49±0.40 ng/ml. In a study by Bideci et al.[23] with 101 cases in our country, C-peptide level was found to be 0.76±0.6 (ng/ml). In our study, the C-peptide level was found to be 0.58±0.62 (ng/ml), similar to the literature. Studies have shown that high HbA1c levels and low C-peptide levels are risk factors for DKA.[24]

In a study by Xin et al.[22]; mean blood sugar at diagnosis was 376.2±154.8 mg/dL, mean HbA1c was 12.7%±2.5, mean C-peptide was 0.49±0.40 ng/ml, the mean insulin was 3.17±2.33 mU/L. In a study conducted by Demir et al.[20] in Istanbul, the mean blood glucose level at the time of diagnosis was reported as 444.7±157.1 mg/dL, and the mean HbA1c was 10.5±2.6%. We have obtained similar results to other studies.

When patients with type 1 DM were examined in terms of dyslipidemia (DLP), the frequency of dyslipidemia was found to be 7.4% in a study by Akyürek et al.[25] In a study by Zambrana-Calvi et al.[26], 1.1% of the cases had HDL <40 mg/dl, 34.4% had LDL >100 mg/dl, 2.2% had TG>150 mg/dl. It was found above.[26] In our study, the frequency of DLP was found to be 5.05%. In our study, the mean TG level was 119.6±88.28 mg/dl, HDL cholesterol level was 56.69±15.41 mg/dl, and LDL cholesterol level was 89.53±25.13 mg/dl.

When patients with type 1 DM were evaluated in terms of vitamin D, in a study conducted by Pozzilli et al.[27] in which they were compared with a new type 1 DM diagnosis control group, average 1.25-OH D levels were found to be lower in patients with diabetes. In a study conducted by Svoren et al.[28] in patients with type 1 DM, vitamin D levels were deficient in 15% (deficiency level was <20 ng/ml), 61% were insufficient (20-30 ng as deficiency level). /ml) was found to be sufficient in 24% of patients. When the vitamin D levels of the patients in our study were examined, the vitamin levels of 39 patients who participated in our study were examined. The rate of patients with vitamin D deficiency (<20 ng/dl) among the patients whose levels were checked was 74.4% and the rate of patients with normal vitamin D levels (>20 ng/dl) was 25.6%.

In type 1 DM, one or more of the insulin autoantibody (IAA), islet cell antibody (ICA), glutamic acid decarboxylase antibody (anti-GAD) and tyrosine phosphatase antibody (IA-2) are mostly positive at the time of diagnosis.17 Louraki et al.[29] found that anti-GAD positivity was 62.4%, IA-2 positivity was 58.8%, and both antibodies were positive together in 42.4%. In the study of Kawasaki 30, anti-GAD positivity was found in 83%, IA-2 positivity in 78%, IAA positivity in 49%, and no autoantibodies were detected in 10% of cases. In a study by Demir et al.[20], anti-GAD was positive in 70.6%, ICA positive in 44.4%, and IAA positive in 42.6%. In a study by Kocabaş et al.[31] they found anti-GAD (69.4%), ICA (28.5%), and IAA (25.5%). In our study, auto-antibodies were not examined in all patients, and this could not be done because of the lack of laboratory facilities in our hospital, the absence of a pediatric endocrinology department, and in cases identified and referred from the emergency services and polyclinics, either not being requested under emergency conditions or repetitive requests being avoided. Insulin autoantibody examined in our hospital was found to be positive in 20 (52.6%) of 38 patients included in the study. This rate is higher than other studies and may not reflect the true rate, as not all diagnosed diabetes patients were examined.

Considering the frequency of diagnosis of patients with type 1 DM, the most common form of admission to the hospital is diabetic ketoacidosis, this rate varies between 15-70% in studies.[32] In a multicenter study by Klingensmith et al.[33] conducted in the USA in 2013 with 805 cases, the frequency of DKA at the time of diagnosis was found to be 34%. In a study by Demir et al.[34] it was found to be 41%. In our study, it was observed that 17.2% (n:17) of the cases presented with DKA. The relatively low rate in our results is due to the fact that there was no pediatric endocrine department in our center for 4 years, and in this case, patients with DKA were referred to another center via the 112 emergency service from the center they first applied.

Considering the mean age of patients presenting with DKA, in a study by Burcul et al.[35], the mean age at presentation with DKA was 9.9±4.8 years. In a study by Bui et al.[36] the mean age at presentation with DKA was 7.8±4.9 years. In our study, the age of admission was found to be 11.23±4.58, and we think that this increase was due to the fact that mild and moderate DKA suspected cases were preferred to other centers after 2016, since there was no pediatric endocrinology clinic in our hospital.

No significant differences were found in previous studies conducted in terms of gender in patients with Type 1 DM presenting with DKA.[37-39] In our study, 41.9% of the patients presenting with DKA were male and 58.1% female, and it was not found to be statistically significant (p:0.508).

Considering the relationship between DKA and blood glucose, in a study conducted by Vicinanza et al.[40], blood glucose levels were found to be statistically significant between patients presenting with DKA and patients not presenting with DKA. (p=0.001). In a study by Sağlam et al.[41] the mean blood glucose level of DKA patients was found to be 473.09±141.04 mg/dl. In our study, blood glucose was found to be 460.58±157.71 mg/dl in accordance with the literature, and the blood glucose levels of the patients presenting with DKA were found to be statistically significant (p=0.001).

Considering the relationship between DKA and HbA1c,

in a study conducted by Hanas et al.[40] on patients presenting with recurrent attacks, the mean HbA1c was found to be statistically significant compared to those who applied once (p=0.004). In the study conducted by Vicinanza et al.[39] there was a statistically significant difference between the mean HbA1c values of the patients presenting with DKA and those presenting without DKA (p<0.001).

CONCLUSION

Investigating the regional characteristics of the disease is guiding in terms of genetic and environmental factors that have an important place in the etiology. The findings of our study were found to be consistent with similar studies and literature.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Kırıkkale University Medical Faculty Clinical Researches Ethics Committee (Date: 08.07.2021, Decision No: 2021.07.09).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Svoren BM, Nicholas J. Diabetes mellitus in children. Kliegman RM, Stanton BF, St Geme JW, Schor NF, Behrman RE (Eds.). Nelson Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier Saunders; 2016:2760-2783.
2. Weber DR, Jospe N. Classification of Diabetes Mellitus. Kliegman RM, Stanton BF, St Geme JW, Schor NF, editors. Nelson Textbook of Pediatrics.21th ed. Philadelphia: Elsevier Saunders;2019:11814-11822.
3. Maniatis AK, Goehrig SH, Gao D, Rewers A, Walravens P, Klingensmith GJ. Increased incidence and severity of diabetic ketoacidosis among uninsured children with newly diagnosed type 1 diabetes mellitus. *Pediatr Diabetes*. 2005;6(2):79-83.
4. Mayer-Davis EJ, Kahkoska AR, Jefferies C, et al. ISPAD clinical practice consensus guidelines: definition, epidemiology, and classification of diabetes in children and adolescents. *Pediatric Diabetes*, 2018;19(Suppl 27):7-19.
5. American Diabetes of Association. Classification and Diagnosis of Diabetes: standards of medical care in diabetes. *Diabetes Care*. 2019;42(1):13-28.
6. Redondo MJ, Foster NC, Libman IM, et al. Prevalence of cardiovascular risk factors in youth with type 1 diabetes and elevated body mass index. *Acta Diabetol*. 2016;53(2):271-277.
7. Singh P, Seth A, Kumar P, Sajjan S. Coexistence of celiac disease & type 1 diabetes mellitus in children. *Indian J Med Res*. 2017;145(1):28-32.
8. Rica I, Mingorance A, Gómez-Gila AL, et al. Achievement of metabolic control among children and adolescents with type 1 diabetes in Spain. Acta Diabetologica, 2017;54(7):677-683.
9. Demir F, Gunoz H, Saka N, et al. Epidemiologic features of type 1 diabetic patients between 0 and 18 years of age in İstanbul city. *J Clin Res Pediatr Endocrinol*. 2015;7(1):49-56.
10. Yesilkaya E, Cinaz P, Andiran N, et al. First report on the nationwide incidence and prevalence of Type 1 diabetes among children in Turkey. *Diabet Med*. 2017;34(3):405-410.
11. Escobar O, Drash AL, Becker DJ. Managment of the child type 1 diabetes. Lifshitz F(ed). Pediatric Endocrinology. 5th ed. New York:2007;101-121.
12. Acar S, Paketçi A, Gören Y, et al. Tip 1 diabetes mellitus olgularının tanı anındaki demografik, klinik ve laboratuvar özelliklerinin değerlendirilmesi. *Türkiye Çocuk Hast Derg*. 2018;12(3):173-179.
13. Cotellessa M, Barbieri P, Mazzella M, Bonassi S, Minicucci L, Lorini R. High incidence of childhood type 1 diyabetes in Liguria, Italy, From 1989 to 1998. *Diabetes Care*. 2003;26(6):1786-1789.
14. Green A, Sjolie A.K, Eshoj O. Trends in the epidemiology of IDDM during 1970-2020 in Fyn County, Denmark. *Diabetes Care*. 1996;19(8):801-806.
15. Aydoğan ZK, Battal F, Doğan D. Tip 1 diabetes mellituslu olguların tanı ve tedavilerinin retrospektif değerlendirilmesi. *Turk J Diab Obes*. 2021;2:111-117
16. Bayoğlu DS, Akıcı N, Bayoğlu V, Gürbüz T, Nuhoğlu Ç. Tip 1 diyabetli çocukların klinik ve epidemiyolojik özellikleri. *Haydarpaşa Numune Eğitim ve Araştırma Hastanesi Tıp Dergisi*. 2014;54(2):87-92.
17. Saka N. Günöz H, Öcal G, Yordam N, Kurtoğlu S (Editorler). *Pediatrik Endokrinoloji;* Diyabetes mellitus. Ankara: Kalkan Matbaacılık; 2003:415-457.
18. Triolo TM, Armstrong TK, McFann K, et al. Additional autoimmune disease found in 33% of patients at type 1 diabetes onset. *Diabetes Care*. 2011;34(5):1211-1213.
19. Nilsson J, Akesson K, Hanberger L, Samuelsson U. High HbA1c at onset cannot be used as a predictor for future metabolic control for the individual child with type 1 diabetes mellitus. *Pediatr Diabetes*. 2017;18(8):848-852.
20. Demir F, Gunoz H, Saka N, et al. Epidemiologic features of type 1 diabetic patients between 0 and 18 years of age in Istanbul city. *J Clin Res Pediatr Endocrinol*. 2015;7(1):49-56.
21. Taşkın E, Yılmaz E, Kılıç M, Ertuğrul S. İnsüline bağımlı diyabetes mellitusun epidemiyolojik özellikleri. *FÜ Sağ Bil Derg*. 2007;21(2):75-79.
22. Mayer-Davis E, Dabelea D, Crandell J, et al. Nutritional factors and preservation of C-peptide in youth with recently diagnosed type 1 diabetes. *Diabetes Care*. 2013;36(7):1842-1856.
23. Xin Y, Yang M, Chen XJ, Tong YJ, Zhang LH. Clinical features at the onset of childhood type 1 diabetes mellitus in Shenyang, China. *J Paediatr Child Health*. 2010;46(4):171-175.
24. Bideci A, Demirel F, Çamurdan O, Cinaz P. Tip 1 diyabetli çocuklarda ilk başvuru bulgularının değerlendirilmesi. *Çocuk Sağlığı Hast Derg*. 2006;49(2):112-116.
25. Leighton E, Sainsbury CA, Jones GC. A Practical review of C-peptide testing in diabetes. *Diabetes Ther*. 2017;8(3):475-487
26. Akyürek N, Atabek ME, Eklioğlu BS. Tip 1 diabetes mellituslu hastaların uzun dönem izlemi: tek merkez deneyimi. *Türkiye Çocuk Hast Derg*. 2015;9(4):243-247
27. Zambrana-Calví GD, Palomo-Atance E, Gourdet ME, León-Martín A, Ballester-Herrera MJ, Giralt-Muiña, P. Lipid changes and their relationship with vitamin D levels in children under 18 years with type 1 diabetes. *Endocrinologia y Nutricion*. 2016;63(3):126-131.
28. Pozzilli P, Manfrini S, Crinò A, et al. Low levels of 25- hydroxyvitamin D3 and 1,25-dihydroxyvitamin D3 in patients with newly diagnosed type 1 diabetes. *Horm Metab Res*. 2005;37(11): 680-683.
29. Svoren BM, Volkening LK, Wood JR, Laffel LM. Significant vitamin D deficiency in youth with type 1 diabetes mellitus. *J Pediatr*. 2009;154(1):132-134.
30. Louraki M, Katsalouli M, Kanaka-Gantenbein C, et al. The prevalence of early subclinical somatic neuropathy in children and adolescents with type 1 diabetes mellitus and its association with the persistence of autoantibodies to glutamic acid decarboxylase (GAD) and islet antigen-2 (IA-2). *Diabetes Res Clin Pract*. 2016;117:82-90.
31. Kawasaki E. Type 1 diabetes and autoimmunity. *Clin Pediatr Endocrinol*. 2014;23(4):99-105.
32. Kocabaş A, Kocabaş BA, Karagüzel G, Akçurin S. Tip 1 diabetes mellitus olgularımızın antropometrik ve metabolik izlem özelliklerinin değerlendirilmesi. *Türkiye Çocuk Hastalıkları Dergisi*. 2013;7(3):113-118
33. Wolfsdorf J, Glaser N, Sperling M. Diabetic ketoacidosis in infants, children and adolescents. *Diabetes Care*. 2006;29(5):1150-1159
34. Klingensmith GJ, Tamborlane WV, Wood J, et al. Diabetic ketoacidosis at diabetes onset: Still an all too common threat in youth. *J Pediatr*. 2013;162(2):330-334.
35. Demir K, Büyükinan M, Dizdarer C, et al. Tip 1 diyabetli çocuklarda tanıda diyabetik ketoasidoz sıklığı ve ilişkili faktörler. *Güncel Pediatri*. 2010;8(3):52-55
36. Burcul A, Polic K, Bartulovic AM. Characteristics of children with diabetic ketoacidosis treated in pediatric ıntensive care unit: two-center cross-sectional study in croatia. *Medicina*. 2019;55(7):362.
37. Bui TP, Werther GA, Cameron FJ. Trends in diabetic ketoacidosis in childhood and adolescence: a 15-yr experience. *Pediatric Diabetes*. 2002;3(2):82-88.
38. Aminzadeh M, Navidi N, Valavi E, Aletayeb SMH. Childhood onset type 1 diabetes at a tertiary hospital in south-western Iran during 2000-2015: Rapid increase in admissions and high prevalence of DKA at diagnosis. Prim Care Diabetes. 2019;13(1):43-48.

39. Neu A, Willasch A, Ehehalt S, Hub R, Ranke MB. Ketoacidosis at onset of type 1 diabetes mellitus in children–frequency and clinical presentation. Pediatr Diabetes 2003;4(2):77-81.
40. Sağlam H, Eren E, Çakır ED, Yüce N, Yıldız N, Çakır S. Clinical and laboratory characteristics of the children with diabetic ketoacidosis/ Diyabetik ketoasidozla basvuran cocukların klinik ve laboratuvar özellikleri. *J Curr Pediatr*. 2008;7(1):94-99.
41. Vicinanza A, Messaaoui A, Tenoutasse S, Dorchy H. Diabetic ketoacidosis in children newly diagnosed with type 1 diabetes mellitus: Role of demographic, clinical, and biochemical features along with genetic and immunological markers as risk factors. A 20-year experience in a tertiary Belgian center. *Pediatr Diabetes*. 2019; 0(5):584-593.
42. Hanas R, Lindgren F, Lindblad B. A 2-yr national population study of pediatric ketoacidosis in Sweden: predisposing conditions and insulin pump use. *Pediatric Diabetes*. 2009;10(1):33-37.