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Effect of Bisphenol-A on Thyroid Hormones and Some Biochemical Parameters in Children with Juvenile Diabetes

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ABSTRACT

This study aims to investigate the effect of serum Bisphenol A (BPA) levels on thyroid hormones and some biochemical parameters in children with newly diagnosed type 1 diabetes mellitus (T1DM).

A total of 139 people, including 74 patients aged 0-18 years who were newly diagnosed with T1DM, 30 healthy siblings of these patients, and 35 healthy children, were included in the study. BPA, apelin, thyroid stimulating hormone (TSH), free T3 (T3), free T4 (T4), thyroglobulin antibody (anti-TG), thyroid peroxidase antibody (anti-TPO), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, C-peptide and glycosylated haemoglobin (HbA1c) levels were measured in the samples obtained from the volunteers. Serum BPA concentrations were higher in children with T1DM compared to their siblings and healthy children ($p<0.05$). The apelin levels in the patient group were observed to be lower than those in their siblings and the healthy children ($p<0.05$). In all three groups, a negative correlation was identified between BPA and apelin. There was no correlation between BPA and TSH, T3 and T4 levels in all three groups ($p>0.05$). Similarly, no correlation was detected between BPA and total cholesterol, LDL, HDL, triglyceride, C-peptide, HbA1c, anti-TG and anti-TPO ($p>0.05$).

In summary, this study shows that BPA levels were increased and apelin levels were decreased in children with T1DM, with a negative relationship between the two. Taken together, our results suggest that BPA may have a role in the pathogenesis or progression of T1DM. Low apelin may be associated with the progression of T1DM.

Keywords: Apelin, Bisphenol A, Thyroid Hormones, Type 1 Diabetes

Introduction

Type 1 diabetes mellitus (T1DM) is among the most prevalent chronic diseases during childhood. The frequency of this ailment in children globally escalates annually by 3% to 5%, and the underlying causes remain unknown (1). The incidence of T1DM is increasing in children worldwide, and this rapid change cannot be explained only by genetic predisposition. Environmental factors have also been identified as potential contributors to the development of diabetes. Twin investigations and epidemiological research have demonstrated that environmental factors have a pivotal role in instigating autoimmunity and participating in the destruction of beta cells in the development of T1DM (2).

Bisphenol A (BPA) is an artificially manufactured chemical compound extensively employed in the production of polycarbonate plastics and epoxy resins. BPA is found in the structure of feeding bottles, food packages, detergents, toys, eyeglasses and water demijohns used in daily life, and its use is increasing day by day. BPA, released from polycarbonates widely used in the plastic industry due to their durability, has estrogen-like properties. It has been proposed that BPA may lead to many diseases, from obesity to cancer, in all age groups, especially babies and children (3).

Several investigations have suggested a possible connection between BPA concentrations and the development of diabetes. These inquiries have uncovered some evidence that BPA exposure might play a role in the emergence of insulin resistance, obesity and type 2 diabetes mellitus (T2DM) (4). They reported that BPA exposure triggered autoimmunity in an experimental T1DM animal model, and as a result, the development of insulitis and diabetes accelerated in animals (5).

Thyroid hormones called T3 and T4 are secreted from the thyroid gland. The most important task of these hormones is to regulate the body's metabolism.

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The frequency of thyroid dysfunction in T1DM patients is 2-3 times higher than in the general population (6). BPA is known to disrupt normal thyroid function by interfering with cellular signalling and gene transcription. *In vitro* studies have suggested that BPA can bind to thyroid hormone receptors TR-alpha and TR-beta, antagonizing the effect of T3 and suppressing its transcriptional activity (7).

Apelin, an adipokine produced by white adipose tissue, plays a multifaceted role, including influencing insulin sensitivity. It is of particular significance in the context of diabetes mellitus and is associated with variations in insulin resistance. Apelin is believed to play a pivotal role in energy metabolism, and the pathogenesis of diabetes, given that apelin-secreting white adipose tissue acts as an endocrine organ (8).

While epidemiological studies suggest a possible effect of BPA on thyroid hormones in the adult population, there is limited data on its effects in children and adolescents. In addition, more data on the effects of BPA on apelin expression and release are needed in the literature. The relationship between BPA thyroid hormones and apelin is unclear. Therefore, this study focuses on investigating the potential effects of serum BPA levels on thyroid hormones, apelin, and various biochemical parameters in children with newly diagnosed T1DM.

Material and Method

This study involved 74 volunteer patients aged 0-18 who presented at the Gaziantep University Faculty of Medicine Şahinbey Research and Application Hospital Pediatric Endocrinology and Metabolism Department clinic and were newly diagnosed with T1DM. The control group consisted of healthy children of similar age and sex selected from the general paediatric outpatient clinic at the same hospital. One hundred thirty-nine volunteers were included, including 30 healthy siblings of T1DM patients and 35 healthy children. Children with any endocrine disorder, obesity, chronic disease or symptoms of diabetes such as polyuria, polydipsia and polyphagia in the last month were not included in the control group. Every participant underwent a physical examination, during which their weight and height were assessed. Body Mass Index (BMI) of all children was calculated according to the formula: weight (kg)/height (m)^2. Demographical data, in addition to the date of diagnosis, records the current diseases of the patients. Blood samples taken from all volunteers participating in the study between 08.30-09.30 in the morning following a 12-hour fast were collected into serum gel tubes (yellow cap) and tubes containing Ethylenediamine tetraacetic acid (EDTA) (purple cap). HbA1c was measured from blood samples taken into EDTA tubes on the same day. Blood samples taken into gel serum tubes were left to clot for approximately 20 minutes at room temperature. After clotting, the samples were centrifuged at 4000 rpm for 20 minutes, and the serum component was collected and stored in labelled Eppendorf tubes at -80 ºC until the study day. It's worth noting that BPA-free materials were used to collect samples from all participants.

Participants and their families were provided with comprehensive information about the study, and written consent to participate was obtained from them. This study received approval from the Gaziantep University Clinical Research Ethics Committee under decision number 2020/228, dated August 27, 2020.

Determination of Biochemical Parameters: Serum levels of total cholesterol, LDL, HDL, and triglycerides were assessed using an enzymatic colourimetric test method. These measurements were conducted on the Beckman Coulter AU5800 autoanalyzer, utilizing commercial kits provided by Beckman Coulter. To determine serum levels of TSH, anti-TG, anti-TPO, T4, and T3, a chemiluminescence immunoassay (CLIA) method was employed. The Beckman Coulter DxI 800 autoanalyzer, in conjunction with Beckman Coulter's commercial kits, measured these analyses. For the assessment of serum C-peptide levels, a chemiluminescence immunoassay (CLIA) method was utilized. The Siemens Immulite 2000 XPI autoanalyzer, in tandem with Siemens' commercial kits, enabled the measurement of C-peptide levels. The percentage of HbA1c in whole blood was determined through a high-performance liquid chromatography (HPLC) method. This analysis was conducted using the Bio-Rad VARIANT II TURBO device, with the assistance of commercial kits from Bio-Rad. Enzyme-linked immunosorbent assay (ELISA) methods were employed to measure serum levels of BPA and Apelin. These assessments utilized commercially available kits specifically sourced from the Bioassay Technology Laboratory in China.

Statistical Analysis: The suitability of the data for normal distribution was tested with the Shaphiro-Wilk test. One-way analysis of variance and LSD multiple comparison tests (for normally distributed variables) and Kruskal Wallis and Dunn multiple (for non-normally distributed variables) were used to compare measurements in more than two groups. Mann-Whitney U test was used to compare non-normally distributed variables between 2 groups. Relationships between categorical variables were tested with the Chi-square test, and relationships between numerical

variables were tested with the Spearman correlation coefficient. The analysis used SPSS for Windows version 22 program, and P<0.05 was considered significant.

Results

Study Population: The study encompassed a total of 74 patients who had been recently diagnosed with T1DM, 30 healthy siblings of these T1DM patients within the same age group, and 35 healthy individuals as healthy controls. The attributes of the study population are delineated in both Table 1 and Table 2. When we analyzed the data, comparing the three groups - the T1DM patients, their siblings, and the healthy controls - in terms of average age and body mass index (BMI), no statistically significant differences were observed between these groups. The p-values were 0.152 for age and 0.054 for BMI (Table 1). Similarly, when examining gender distribution and age categories across the groups, no statistically significant differences were identified (Table 2).

Evaluation of BPA level: Significant disparities were evident in the levels of BPA when comparing the patient, their relatives, and the healthy control group (p=0.001), as displayed in Table 3. The BPA levels in the patient group were significantly and statistically higher than those in the patient-relative group (p=0.010). Furthermore, the BPA levels in the patient group also exhibited a statistically significant increase when contrasted with those in the healthy control group (p=0.001). Conversely, no significant variation in BPA levels was detected among the patient-relative group and the healthy control group, with a p-value of 0.654.

Evaluation of TSH, T3, T4, Anti-TPO and Anti-TG levels: There was no significant variation in thyroid-stimulating hormone (TSH) values when comparing the patient group, patient-relative group, and healthy control group (p=0.705), as indicated in Table 3.

In contrast, there were statistically significant differences in free triiodothyronine (free T3) levels among these three groups (p=0.034), also presented in Table 3. The patient group exhibited significantly lower free T3 levels when compared to the healthy control group (p=0.011). Nonetheless, no significant distinctions were noted between the patient group's free T3 levels and those of their relatives (p=0.127). Similarly, no significant differences were detected when comparing free T3 levels between the patient-relative group and the healthy control group (p=0.414). Moreover, they displayed significant disparities in T4 levels among the patient group, patient-relative group, and healthy control group (p=0.004) (Table 3). The patient group had markedly lower free T4 levels than the healthy control group (p=0.001). No statistically significant variances were observed between the patient group's free T4 levels and the patient-relative group's free T4 levels (p=0.167). Likewise, a significant difference was not observed between the patient-relative group's free T4 levels and the healthy control group's free T4 levels (p=0.110).

When comparing the patient, patient relative and healthy groups in terms of anti-TPO positivity and anti-TG positivity, a statistically significant difference was detected between the groups (p = 0.001 and p = 0.001, respectively) (Table 4). The patient group had a higher occurrence of anti-TPO positivity and anti-TG positivity in comparison to both the patient-relative and healthy groups (p = 0.001 and p = 0.001, respectively).

Evaluation of apelin level: A significant contrast was evident in the levels of apelin when comparing the patient group, their relatives, and the healthy control group (p=0.001), as detailed in Table 3. The levels of apelin in the patient group were significantly lower than those in the patient-relative group (p=0.001). Furthermore, the apelin levels in the patient group exhibited a statistically significant decrease when contrasted with those in the healthy control group (p=0.001). However, a significant difference was not detected between the apelin levels of the patient-relative group and the apelin levels of the healthy control group (p=0.771).

Evaluation of lipid profile: A noteworthy and statistically significant difference was observed among the patient, the patient-relative, and the healthy control group according to total cholesterol levels (p=0.003), as detailed in Table 3. When the data are analyzed in more detail, a significant increase in total cholesterol levels is revealed within the patient groups compared to the closely related group (p=0.019). Additionally, it's noteworthy that the patient group exhibited significantly elevated total cholesterol levels in comparison to the healthy control group (p=0.001). However, no significant disparity was found between the total cholesterol levels of the patient-relative group and the healthy control group, with a p-value of 0.314.

Moreover, a significant difference was evident when comparing the patient group, their relatives and the healthy control group in terms of LDL levels (p=0.005), as illustrated in Table 3. It was established that the patient group had significantly higher LDL levels than the healthy control group (p=0.001). Notably, there was no statistically notable distinction in LDL levels between the patient group and the patient-relative group (p=0.061). Likewise, there was

Table 1: Comparison of Groups In Terms of Age and BMI

	Patient (n=74)	Patient's relative (n=30)	Healthy (n=35)	
Variables	Mean±SD	Mean±SD	Mean±SD	P
Age (Years)	9.24 ± 4.56	9.31 ± 4.73	7.45 ± 5.12	0.152
BMI (kg/m²)	18.02 ± 3.11	16.7 ± 2.87	16.81 ± 3.08	0.054

One-way ANOVA. SD: Standard Deviation

Table 2: Comparison of Groups In Terms of Gender and Age Class

		Patient (n=74)	Patient's relative (n=30)	Healthy (n=35)	P
		n (%)	n (%)	n (%)	
Gender	Male	37 (50)	15 (50)	14 (40)	0.592
	Woman	37 (50)	15 (50)	21 (60)	
Age class (Years)	≤6 age	21 (28.4)	9 (30)	14 (40)	0.465
	>6 age	53 (71.6)	21 (70)	21 (60)	

Chi-square test

no statistically significant difference in LDL levels between the patient-relative group and the healthy control group, with a p-value of 0.146.

In addition, a significant distinction was identified in the high-density lipoprotein (HDL) levels among the patient group, patient relatives, and the healthy control group (p=0.001), as outlined in Table 3. The HDL levels in the patient group were significantly lower than those in the patient-relative group (p=0.004). Furthermore, the HDL levels in the patient group exhibited a statistically significant decrease when compared to those in the healthy control group (p=0.001). Similarly, the HDL levels in the patient-relative group were statistically significantly lower than those in the healthy control group (p=0.038).

Lastly, a statistically significant difference was observed in triglyceride levels among the patient group, their relatives, and the healthy control group (p=0.001), as outlined in Table 3. The triglyceride levels in the patient group were significantly and statistically higher than in the patient-relatives group (p=0.001). Moreover, the triglyceride levels in the patient group exhibited a significant increase when compared to those in the healthy control group (p=0.001). Conversely, no significant variation was detected in triglyceride levels between the patient-relative group and the healthy control group, with a p-value of 0.618.

Evaluation of C-peptide level: The assessment of C-peptide levels revealed a statistically significant difference among the patient, the patient-relative, and the healthy control group (p=0.001), as delineated in Table 3. The C-peptide levels in the patient group were significantly and statistically lower than those in the patient-relative group (p=0.001). Moreover, a significant decrease in C-peptide levels was noted in the patient group when compared to the healthy control group (p=0.001). Additionally, it was observed that the C-peptide levels in the group of patients' relatives were significantly lower than those in the healthy control group (p=0.029).

Evaluation of haemoglobin A1c level: In the evaluation of HbA1c levels, a statistically significant distinction emerged between the patient group, the patient-relative group, and the healthy control group (p=0.001) (Table 3). A more detailed analysis of the data revealed that the HbA1c levels in the patient were markedly and statistically higher than those in the patient-relative group (p=0.001). Furthermore, the HbA1c levels in the patient group exhibited a significant increase compared to those in the healthy control group (p=0.001). Importantly, no difference was detected between the HbA1c levels in the patient-relative group and those in the healthy control group (p=0.952).

Relationship Between BPA and Demographic and Clinical Variables in Patients: Regarding BPA levels, a notable statistical discrepancy was identified, with higher BPA levels in patients aged ≤6 years compared to patients aged >6 years (p=0.009). Additionally, BPA levels in patients admitted during the hot season were significantly higher than those admitted during the cold season (p=0.006) (Table 5). However, no significant differences were observed in BPA levels concerning gender, puberty, C-peptide, anti-TPO positivity, and anti-TG positivity among the patients (p=0.310, p=0.180, p=0.378, p=0.950, p=0.677) (Table 5).

Evaluation of the Relationship Between BPA and Apelin: In the context of the relationship between BPA and apelin, a moderate negative correlation was

Table 3: Comparison of TSH, T3, T4, HbA1c, C-peptide, Total Cholesterol, LDL, HDL, Triglyceride, BPA and Apelin Levels Between Groups

	Patient (n=74)	Patient's relative (n=30)	Healthy (n=35)	
Variables	Mean ± SD	Mean ± SD	Mean ± SD	P
HbA1c (%)	12.61 ± 2.96	5.31 ± 0.32	5.27 ± 0.45	0.001*
Free T4 (ng/dL)	0.92 ± 0.28	0.99 ± 0.17	1.08 ± 0.16	0.004*
TSH (mU/L)	2.39 ± 2.22	2.21 ± 1.11	2.19 ± 0.99	0.705
	Median [25%-75%]	Median [25%-75%]	Median [25%-75%]	
C-peptide (µg/L)	0.31 [0.16-0.58]	1.31 [0.87-1.93]	2.21 [1.53-3]	0.001*
Free T3 (pg/mL)	3.36 [2.96-4.04]	3.64 [3.53-4]	3.86 [3.39-4.11]	0.034*
Total cholesterol (mg/dL)	175 [149-219]	154.5 [135-172]	150 [134-165]	0.003*
LDL-cholesterol (mg/dL)	102.5 [94-127]	93.5 [78-110]	90 [77-103]	0.005*
HDL-cholesterol (mg/dL)	41 [34-48]	48.5 [43-56]	54 [50-58]	0.001*
Triglyceride (mg/dL)	161 [107-273]	74.5 [62-97]	69 [55-85]	0.001*
Bisphenol A (ng/mL)	72.34 [66.63 -87.19]	49.23 [45.12-87.17]	53.17 [18.22-96.1]	0.001*
Apelin (ng/L)	175.87 [143.52-230.54]	217.56 [186.49-416.44]	296.62 [148.03-740.49]	0.001*

*p <0.05 statistically significant. One-way analysis of variance (HbA1c and Free T4) and Kruskal Wallis test (TSH, C-peptide, Free T3, Total cholesterol, LDL-cholesterol, HDL-cholesterol, Triglyceride, Bisphenol A and Apelin). SD: Standard Deviation

Table 4: Comparison of Groups In Terms of Anti-TPO and Anti-TG Positivity

		Patient	Patient's relative	Healthy	
		n(%)	n(%)	n(%)	P
Anti-TPO	Positive	10 (15.9)	0 (0)	0 (0)	0.001*
	Negative	53 (84.1)	30 (100)	35 (100)	
Anti-TG	Positive	6 (10.3)	0 (0)	0 (0)	0.001*
	Negative	52 (89.7)	30 (100)	35 (100)	

*p <0.05 statistically significant. Chi-square test

established between these two variables in the patient group, patient-relative group, and healthy control group (r=-0.414, p=0.001; r=-0.502, p=0.008; r=-0.424, p=0.017, respectively), as seen in Table 6. Conversely, no significant correlations were observed between BPA and other variables across all three groups (Table 6).

Discussion

T1DM is a disease characterized by inadequate secretion of insulin and hyperglycemia due to pancreatic beta cell destruction, mostly due to autoimmune mechanisms (9). It has been suggested that many factors are responsible for the development of T1DM and that environmental factors trigger the autoimmune process in people with genetic predisposition (10).

BPA is a synthetically produced chemical substance widely used in producing epoxy resins and polycarbonate structured plastics (4). In many studies, BPA has been described as an endocrine-disrupting chemical (EDC) due to its estrogenic properties and has been found to bind and activate the estrogen receptor (ER) in humans (11). BPA is one of the most produced chemicals worldwide due to its many applications (4). It has been suggested that BPA can cause many diseases, from obesity to cancer, in all age groups, especially infants and children (3).

Predictions that BPA is associated with diabetes have been obtained from animal studies and *in vitro* experiments. There is a limited amount of research investigating the relationship between T1DM and BPA in humans. The relationship between them has been examined through epidemiological studies, but contradictory results have been obtained. An investigation assessed the potential association between T1DM and BPA exposure by contrasting the urinary BPA concentrations of children monitored with T1DM with those of the control group. While the urinary BPA concentration in the T1DM group was numerically greater than that of the control group, statistical significance was not observed (4). A

Table 5: Relationship Between BPA and Demographic and Clinical Variables in Patients

			Bisphenol A (ng/mL)	
Variables		n	Median[25%-75%]	P
Age class (Years)	≤6 age	15	92.18 [72.8 -131.35]	0.009*
	>6 age	52	70.81 [66.39 -80.49]	
Gender	Male	33	72.8 [67.64 -87.42]	0.310
	Woman	34	71.1 [66.16 -82.24]	
Puberty	Yes	39	71.59 [66.47 -80.72]	0.180
	No	28	76.76 [67.38 -99.13]	
C-peptide (µg/L)	Positive	21	71.59 [68 -72.8]	0.378
	Negative	45	76.3 [66.31 -92.18]	
Anti-TPO (lU/mL)	Positive	10	71.01 [66.63 -78.38]	0.950
	Negative	47	72.27 [66.16 -82.24]	
Anti-TG (lU/mL)	Positive	6	71.01 [66.63 -76.3]	0.677
	Negative	48	72.27 [65.95 -83.87]	
Application season	Cold	31	68.04 [62.4 -76.4]	0.006*
	Hot	36	78.97 [69.57 -93]	

*p <0.05 statistically significant. Mann-Whitney U test

separate investigation indicated that BPA exposure could impact the β-cells in the pancreas and encourage autoimmunity, expediting the development of insulitis and diabetes in an animal model of T1DM (12). An additional research effort investigated the connection between urinary BPA levels and T1DM in children and adolescents. The study revealed that the T1DM group had significantly higher urinary BPA levels compared to the control group (13).

In this study, planned as a case-control study, we compared the serum BPA levels of patients newly diagnosed with T1DM in the 0-18 age group with the serum BPA levels of the patients' siblings and healthy children. In the study, serum BPA values of newly diagnosed children with T1DM were significantly higher than their siblings and healthy children. In contrast, no significant difference was found when the serum BPA values of the patient's siblings and healthy children were compared. This result is crucial as it shows the relationship between T1DM and BPA, which must be clinically clarified. We think that the serum BPA levels of T1DM patients being found to be significantly higher than their siblings despite sharing the same environment may be due to the individuals' daily habits, the amount of BPA contained in the materials they come into contact with, the frequency of contact, the different exposure times, and the suppressed BPA metabolism in the patient individuals. Although this study was cross-sectional, an attempt was made to reveal a causal relationship between BPA and T1DM by including siblings who share the same environment. However, the fact that the BPA values of the patient siblings' group and the healthy children group were similar did not confirm this possible causality. The complexity of the pathogenesis of T1DM and the different results obtained in clinical studies have made us think it is challenging to reveal the possible relationship between BPA and T1DM.

Emerging evidence indicates a close relationship between apelin and diabetes as well as diabetic complications. Numerous studies have suggested that apelin treatment during insulin resistance initiates a series of coordinated beneficial effects, including reducing hyperinsulinemia and adiposity stimulating glucose uptake and utilization (14). Apelin has been shown to enhance overall insulin sensitivity in skeletal muscle *in vitro* and in animal models (15). Additionally, apelin is believed to normalize diabetes-induced renal hypertrophy, kidney inflammation, and albuminuria (16).

Epidemiological studies have attempted to examine the relationship between apelin hormone and diabetes, but contradictory results have been obtained. In a study conducted with children with T1DM, the patients displayed significantly elevated plasma apelin levels compared to the control group (17). In another study, the plasma apelin concentrations in children with T1DM were markedly elevated compared to those in the control group (18).

In another study in the literature, the serum apelin levels of patients with T1DM were contrasted with those of the control groups. Contrary to the previous two studies, the serum apelin concentrations in children with T1DM were substantially lower

Table 6: Correlation Analysis Between BPA and Other Variables In All Groups

		Patient	Patient's relative	Healthy
		Bisphenol A (ng/mL)	Bisphenol A (ng/mL)	Bisphenol A (ng/mL)
Age (Years)	r	-0.216	-0.249	-0.052
	p	0.079	0.201	0.781
BMI (kg/m²)	r	-0.083	0.397	-0.014
	p	0.588	0.128	0.947
HbA1c (%)	r	-0.162	0.152	-0.032
	p	0.193	0.441	0.864
C-peptide (µg/L)	r	-0.200	0.081	0.127
	p	0.107	0.682	0.497
Free T3 (pg/mL)	r	0.135	0.191	-0.061
	p	0.360	0.330	0.743
Free T4 (ng/dL)	r	-0.098	0.302	0.162
	p	0.451	0.118	0.383
TSH (mU/L)	r	-0.042	0.162	0.237
	p	0.757	0.410	0.199
Total cholesterol (mg/dL)	r	0.010	-0.277	-0.053
	p	0.964	0.154	0.779
LDL-cholesterol (mg/dL)	r	-0.105	-0.220	0.095
	p	0.661	0.260	0.610
HDL-cholesterol (mg/dL)	r	0.201	-0.155	0.121
	P	0.409	0.430	0.515
triglyceride (mg/dL)	r	-0.120	0.182	-0.135
	p	0.606	0.354	0.470
Apelin (ng/L)	r	-0.414	-0.502	-0.424
	p	0.001*	0.008*	0.017*

*p <0.05 statistically significant. r: Spearman rank correlation coefficient

compared to those in the control group (19). Similarly, in our study, which attempted to determine the relationship between serum apelin concentrations in newly diagnosed T1DM patients, their siblings and healthy children, it was found that the serum apelin levels of the patient group were statistically significantly lower than those of their siblings and healthy children.

Research indicates that BPA influences the expression of adipokines. As an illustration, BPA reduced adiponectin expression while boosting leptin expression in 3T3-L1 adipocytes, with no impact on the resistin mRNA level (20). Apelin is a peptide hormone that has recently been added to the family of adipokines. As a result of our literature review, we did not find any studies investigating the relationship between BPA and apelin in diabetic patients. One of the aims of the study is to investigate the effect of BPA on apelin expression in T1DM patients. Therefore, we investigated the correlation between serum BPA concentrations and serum apelin concentrations in T1DM patients. Our own research showed a moderate negative association between serum BPA levels and serum apelin levels in children in all three groups. Considering that apelin is an adipokine with anti-diabetic properties, our results suggest that BPA and apelin may be associated with the development of T1DM.

In conclusion, the study demonstrated that serum BPA levels were elevated while serum apelin levels were decreased in children newly diagnosed with T1DM. Furthermore, a moderate negative correlation between BPA and apelin levels was identified, indicating a potential association between BPA and apelin in the development of T1DM. Taken together, our results suggest that BPA may have a role in the pathogenesis or progression of T1DM. Low apelin may be associated with the progression of T1DM. However, the authors suggest that further insights can

be gained through prospective studies and investigations involving larger sample sizes.

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Competing Interests: The authors declare no conflicts of interest related to this article.

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Data Availability: Data will be made available on request.

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