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Assessing Oral Glucose Tolerance Test in Children with Cystic Fibrosis

Kistik Fibrozisli Çocuklarda Oral Glikoz Tolerans Testi Değerlendirmesi

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Abstract

Background: The objective of this study is to determine the presence and frequency of cystic fibrosis- related diabetes (CFRD) and abnormal glucose tolerance (AGT) in children with cystic fibrosis (CF) across various age groups using an oral glucose tolerance test (OGTT), and to evaluate their association with nutritional status.

Materials and Methods: Twenty-five patients diagnosed with CF underwent a standard 2-hour OGTT while in a clinically stable period. Plasma glucose and insulin levels were measured. Patients were categorised as normal glucose tolerance (NGT), indeterminate glucose tolerance (INDET), impaired glucose tolerance (IGT), CFRD or impaired fasting glucose (IFG). All classifications other than NGT were categorized as AGT. Clinical and anthropometric data was recorded, and all statistical analyses performed using SPSS 23.

Results: In the present study, 60% of the subjects were female. The mean chronological age at which the OGTT was performed was 9.44 ± 5.36 years (min 1.2 years). None of the patients had fasting hyperglycaemia. NGT was detected in 12 patients (48%), and AGT in 13 patients (52%). Of the 25 CF patients, 5 (20%) were diagnosed with CFRD, 2 (8%) of whom were less than 10 years old at the time of their diagnosis. The patients with AGT had a lower mean body weight standard deviation (SD) and body mass index SD than those with NGT.

Conclusions: The findings of this study suggest that the possibility of CFRD and AGT should be considered in the context of CF, and that screening with an OGTT may be necessary starting at age five. Weight loss and failure to gain weight may be early signs of CFRD and AGT.

Keywords: Abnormal Glucose Tolerance, Cystic Fibrosis, Cystic Fibrosis-Related Diabetes, Oral Glucose Tolerance Test

Öz

Amaç: Bu çalışmanın amacı, oral glikoz tolerans testi (OGTT) ile çeşitli yaş gruplarındaki kistik fibroz (KF) hastası çocuklarda kistik fibrozis ilişkili diyabet (KFİD) ve anormal glikoz toleransı (AGT) durumlarının varlığını ve sıklığını tespit etmek, beslenme durumu ile ilişkisini değerlendirmektir.

Materyal ve metod: Kistik fibroz tanısı konmuş 25 hastaya klinik olarak stabil dönemde iken standart 2 saatlik OGTT yapıldı. Plazma glikoz ve insülin düzeyleri ölçüldü. Hastalar normal glikoz toleransı (NGT), indetermine glikoz toleransı (İNGT), bozulmuş glikoz toleransı (BGT), KFİD veya bozulmuş açlık glikozu (BAG) olarak sınıflandırıldı. Normal glikoz toleransı, dışındaki tüm sınıflandırmalar AGT olarak kategorize edildi. Klinik ve antropometrik veriler kaydedildi ve tüm istatistiksel analizler SPSS 23 kullanılarak gerçekleştirildi.

Bulgular: Bu çalışmada, deneklerin %60'ı kadındı. OGTT'nin uygulandığı ortalama kronolojik yaş 9.44 ± 5.36 yıldı (min. 1.2 yıl). Hiçbir hastada açlık hiperglisemisi görülmedi. Hastaların 12'sinde (%48) NGT, 13'ünde (%52) AGT saptandı. Çalışmaya katılan 25 KF hastasından 5'ine (%20) KFİD tanısı konuldu; bunların 2'si (%8) tanı anında 10 yaşından küçüktü. AGT'li hastaların ortalama vücut ağırlığı standart sapması (SD) ve vücut kitle indeksi SD'si, NGT'li hastalara göre daha düşüktü.

Sonuç: Çalışma, KF'de KFİD ve AGT olasılığının göz önünde bulundurulmasını ve beş yaşından itibaren OGTT ile tarama yapılmasının gerekli olabileceğini göstermektedir. Kilo kaybı ve kilo alamama, KFİD ve AGT'nin erken belirtileri olabilir.

Anahtar Kelimeler: Anormal glikoz toleransı, Kistik fibrozis, Kistik fibrozis ile ilişkili diyabet, Oral glikoz tolerans testi

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Introduction

Cystic fibrosis (CF) is the most prevalent autosomal recessive disorder, with prevalence figures standing at approximately one in 3,500 newborns (1). Cystic Fibrosis-Related Diabetes (CFRD) is a common complication of CF. Its prevalence rises with age, from 5-10% in children to 40-50% in adults (2,3). At the onset of the course, CFRD may be asymptomatic, and consequently identified solely through routine screening. Typically, progression occurs in a gradual manner, with the majority of patients exhibiting clinical decline, manifesting as unexplained, chronic reductions in pulmonary function and deteriorating nutritional status, prior to the manifestation of classic diabetic symptoms (4). The presence of subclinical hyperglycaemia has been demonstrated to exacerbate pulmonary disease through the promotion of infection and inflammation, consequently leading to an increased frequency of pulmonary exacerbations, a decline in FEV1, and an escalation in hospitalization rates (5). It has been observed that abnormal glucose tolerance (AGT) associated with CF may develop at an early age and is linked to increased morbidity and mortality (6).

The pathophysiology of AGT associated with cystic fibrosis involves not only partial loss of β-cells and disrupted insulin secretion, but also insulin resistance linked to chronic inflammation. These factors contribute to progressive insulin deficiency and lead to indeterminate glycemia (INDET), impaired glucose tolerance (IGT), impaired fasting glucose (IFG) and, ultimately, prediabetic and diabetic clinical conditions such as CFRD (7-10).

The oral glucose tolerance test (OGTT) is the standard screening tool recommended on an annual basis for the detection of CFRD in children, beginning at age ten, in accordance with current guidelines (11,12). The utilisation of OGTT has facilitated the identification of AGT and its subtypes, including CFRD, IGT, INDET and IFG. It is imperative to initiate these interventions at the earliest stage of the patient's life, encompassing IGT and INDET. Research has indicated that a considerable proportion of children diagnosed with CF demonstrate AGT, despite displaying normoglycaemia during fasting periods (13,14). Fasting hyperglycaemia (FH) has been observed to manifest in the advanced stages of CFRD, concurrently with the onset of elevated haemoglobin A1c (HbA1c) levels (15).

A robust association has been identified between CFRD and nutritional status, with declines in nutritional indices typically preceding the diagnosis of CFRD (5). Insulin is a potent anabolic hormone that is indispensable for preserving lean body mass. Its deficiency, in conjunction with exocrine pancreatic insufficiency, malabsorption, and elevated energy expenditure due to respiratory effort, precipitates a catabolic state that contributes to suboptimal nutritional outcomes in individuals with CFRD (5).

Early detection of AGT and the implementation of appropriate interventions are of paramount importance, as a diagnosis of CFRD is associated with impaired lung function and an increased mortality rate (9,10,16-18). However, current guidelines recommend that an OGTT be performed for the diagnosis of AGT from the age of ten onwards (11,12). However, the fact that AGT screening does not take place until the age of ten means that opportunities for early diagnosis and intervention are being missed. Estimates suggest that AGT affects one in three children diagnosed with cystic fibrosis, yet it is significantly underdiagnosed in this age group (6).

The aim of this study is to determine, in a cross-sectional study, the presence and diversity of AGT associated with the OGTT test, as well as the nutritional status, in children of different ages with clinically stable cystic fibrosis who are being followed at our clinic.

Material and Method

Study Design and Subjects

This single-centre, cross-sectional study was conducted between November 2021 and March 2022 and included 25 patients diagnosed with CF who were being followed up at the paediatric gastroenterology outpatient clinic and who underwent a clinical OGTT by the paediatric endocrinology department during their annual screening. Patients who met the following criteria were excluded from the study: those experiencing an acute pulmonary exacerbation; those receiving systemic steroid therapy for allergic bronchopulmonary aspergillosis; those receiving inpatient treatment; and those with a known history of diabetes. The following data were collated: gender, age at diagnosis, age at the time of study participation, anthropometric measurements (body weight (BW), height, body mass index (BMI)), fasting blood glucose (FBG) levels, insulin, C-peptide, haemoglobin A1c (HbA1c) and oral glucose tolerance test (OGTT) results. The calculation of BMI standard deviation (SD), weight SD and height SD was conducted in accordance with reference values specific to age and sex (19).

The oral glucose tolerance test (OGTT), HbA1c and definitions

All patients underwent a standard 2-hour OGTT. The 2-hour OGTT was performed following an 8-hour fast, during which

patients were given a 1.75 g/kg (maximum 75 g) glucose solution to drink; plasma glucose and insulin levels were measured at 0, 30, 60, 90 and 120 minutes. The diagnosis of diabetes was made on the basis of the following criteria: a fasting serum glucose level of 126 mg/dL or greater, an OGTT 2h serum glucose level of 200 mg/dL or greater, and an HbA1c level of 6.5% or greater (20). In cystic fibrosis, the classification of glucose tolerance is divided into five categories, ranging from normal glucose tolerance to overt diabetes (10). The classification system employed is as follows: normal glucose tolerance (NGT), indeterminate glucose tolerance (INDET), impaired glucose tolerance (IGT), cystic fibrosis-related diabetes (CFRD), and impaired fasting glucose (IFG), provided in Table 1 (10,21,22). The categorisation of glucose tolerance was conducted in accordance with the 2022 International Society for Pediatric and Adolescent Diabetes (ISPAD) Clinical Practice Consensus Guidelines for Cystic Fibrosis-Associated Diabetes (22).

Table 1. Categories of abnormal glucose tolerance in cystic fibrosis

Category	**Fasting plasma glucose before test**	**Plasma glucose 2 hours after ingestion of 1.75 g/kg glucose**
Normal glucose tolerance (NGT)*	<126 mg/dL	<140 mg/dL
Prediabetes categories		
Indeterminate glycemia (INDET)	<126 mg/dL	<140 mg/dL, with a mid-point peak >200 mg/dL
Impaired glucose tolerance (IGT)	<126 mg/dL	140 to 200 mg/dL
CFRD		
CFRD without fasting hyperglycemia	<126 mg/dL	≥200 mg/dL
CFRD with fasting hyperglycemia	≥126 mg/dL	OGTT not necessary
Impaired fasting glucose (IFG)	Fasting glucose levels; 110-126 mg/dl	All glucose levels <200 mg/dL

In the present study, patients' OGTT results were classified according to the definitions provided in Table 1. In the study, the definition of abnormal glucose tolerance (AGT) is all-encompassing in its characterisation of glucose tolerance, with the exception of normal glucose tolerance (NGT) (10).

An HbA1c of 5.7-6.4%, when obtained through a standardised analysis, is indicative of prediabetes (20). A HbA1c level of 6.5% or higher was defined as diabetes (20). The levels of HbA1c in the serum were analysed using high-performance liquid chromatography (HPLC).

Statistical Analysis

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 23. For each continuous variable, data normality was confirmed using the Shapiro-Wilk test. Descriptive statistical methods were used in the evaluation of the study data. The Mann-Whitney U test was used for statistical comparison of nonparametric distributed continuous data. In comparing multiple groups, Kruskal Wallis and One-way ANOVA tests were used according to parametric results. In comparison of categorical variables, Chi-square test was used to compare the categorical variables. A p-value of less than 0.05 was considered statistically significant.

Ethical Approval

The study was approved by the Clinical Research Ethics Committee of University of University of Health Sciences Türkiye Bursa Yüksek İhtisas Training and Research Hospital (approval no:2011-KAEK-25 2021/11-15, date: November 3, 2021).

Results

The study comprised 25 patients diagnosed with cystic fibrosis, 15 (60%) of whom were female. The patients' gender, age at diagnosis, chronological age and anthropometric characteristics are presented in Table 2. The mean chronological age at which the OGTT was performed was 9.44 ± 5.36 years. The youngest patient included in the study was 1.2 years old.

Table 2. Patients' gender, age and anthropometric characteristics	
Number of patients*	**25 (100)**
Gender *	
Female	15 (60)
Male	10 (40)
Age at diagnosis (months)	4.48±7.34 2 (0.5-36)
Calendar age (years)	9.44±5.36 8.2 (1.2-18)
BW (kg)	28.24±15.48 23.5 (8-64)
BW SD	-1.24±1.46 -1.22 (-4.96-1.54)
Height (cm)	128±28.28 130 (72-174)
Height sd	-0.77±1.30 -0.55 (-4.5-1.3)
BMI (kg/m^2)	15.89±2.83 14.7 (12.8-22.5)
BMI SD	-1.19±1.22 -1.45 (-3.22-1.78)
*n (%) BW: Body weight, BMI: Body mass index, SD: Standard deviation Data are presented as mean ± SD and/or median (min–max).	

The mean HbA1c (%), mean C-peptide levels and OGTT results for the patients participating in the study are presented in Table 3. Fasting hyperglycaemia was not detected in any of the patients participating in the study. It was established that the median glucose concentration at the midpoint (i.e. at the 60th minute) was 154 mg/dL (min. 89– max. 288).

Table 3. Patients' HbA1c, C-peptide and OGTT laboratory results	
HbA1c (%)	5.91±0.48 5.9 (5-6.8)
C-peptide (ng/ml)	1.05±0.46 1.8 (0.17-1.91)
Glucose 0 min (mg/dl)	88.68±14.36 85 (58-117)
Glucose 30 min (mg/dl)	156.4±36.13 160 (84-230)
Glucose 60 min (mg/dl)	163±58.68 154 (89-288)
Glucose 90 min (mg/dl)	147±60.81 131 (65-273)

Table 3. Continued	
Glucose 120 min (mg/dl)	126±48.46 115 (66-220)
Insulin 0 min (mU/l)	3.63±1.60 4 (1-7)
Insulin 30 min (mU/l)	20.08±11.07 16 (3-54)
Insulin 60 min (mU/l)	27.4±20.21 23 (2-71)
Insulin 90 min (mU/l)	22.28±15.13 18 (3-63)
Insulin 120 min (mU/l)	18.76±16.60 13 (1-66)
Data are presented as mean ± standard deviation and/or median (min–max)	

The patients were then classified according to their HbA1c levels, resulting in the identification of 3 patients (12%) with a diagnosis of diabetes, 16 (64%) with prediabetes, and 6 (24%) with normal levels. The clinical and laboratory characteristics of the patients, classified according to their HbA1c levels, are presented in Table 4.

Table 4. Classification of patients according to HbA1c, age, gender, anthropometric and laboratory characteristics

	Normal (n=6)	**Prediabetes (n=16)**	**Diabetes (n=3)**	**p**
Calendar age (years)	8.96±6.0	9.05±5.37	12.46±4.8	0.602#
Age at diagnosis (months)	3 (0.5-12)	2 (0.5-12)	8 (1-36)	0.211±
Gender *				
Female	5 (83)	8 (50)	2 (67)	0.353¶
Male	1 (17)	8 (50)	1 (33)	
BW (kg)	27.83±15.47	27.06±16.04	32.5±15.15	0.888#
BW sd	-0.84±1.08	-1.17±1.37	-2.44±2.47	0.303#
Height (cm)	125.8±31.02	126.04±28.98	143.16±22.37	0.634#
Height sd	-0.32±0.69	-1.82±1.11	-1.38±2.95	0.517#
BMI (kg/m2)	15.10 (13.1-1.98)	14.2 (12.8-22.5)	14.2 (13.8-17.5)	0.826±
BMI sd	-0.98±1.11	-1.08±1.26	-2.15±1.13	0.356#
HbA1c (%)	5.28±0.22	6±0.24	6.73±0.11	<0.001#
C-peptide (ng/ml)	1.06±0.63	1.06±0.43	0.95±0.42	0.929#
Normal, HbA1c <5.7%; Prediabetes, HbA1c 5.7%–6.4%; Diabetes, HbA1c ≥6.5% OGTT, Oral Glucose Tolerance Test; BW, Body weight; BMI, Body mass index; sd, standard deviation; HbA1c, Hemoglobin A1c # One-Way ANOVA test, ± Kruskal Wallis test, ¶ Chi-Square test				
Data are presented as mean ± standard deviation and/or median (min–max).				

In the OGTT results of the patients, NGT was observed in 12 (48%) of the 25 patients, whilst AGT was observed in 13 (52%) of the patients. The mean BW SD and mean BMI SD of patients with AGT were found to be significantly lower than those with NGT. Moreover, a comparison of the two groups revealed no significant discrepancy in the mean HbA1c and mean C-peptide values, are presented in Table 5.

Table 5. Categories of glucose tolerance in cystic fibrosis					
	Normal glucose tolerance (NGT) (n=12)	**Prediabetes categories (n=10)**		**Cystic Fibrosis-Related Diabetes (CFRD)**	**p**
		Indeterminate glycemia (INDET) (n=5)	**Impaired glucose tolerance (IGT) (n=5)**	**CFRD without fasting hyperglycemia (n=3)**	
Calendar age (years)	7.73±5.77	10.04±4.55	11.12±5.5	12.5±4.5	0.457#
Age at diagnosis (months)	3.25±2.86	8±15.66	4.8±4.96	3±4.33	0.385±
Gender *					
Female	7 (58)	4 (80)	3 (60)	1 (33)	0.623¶
Male	5 (42)	1 (20)	2 (40)	2 (67)	
BW (kg)	27.4±17.75	28.26±14.7	26.62±14.37	34.3±15	0.793±
BW sd	-0.39±1.10	-1.22±1.06	-3.03±1.34	-1.75±0.75	0.01±
Height (cm)	115.5±31.65	134.04±20.71	129.52±27.61	149.4±22.25	0.409#
Height sd	-0.28±0.75	-0.40±1.16	-2.48±1.63	-1.69±0.36	0.05#
BMI (kg/m^2)	17.04±3.14	14.92±2.47	14.72±2.16	14.9±2.27	0.297#
BMI SD	-0.37±1.14	-1.4±0.82	-2.21±0.58	-2.37±0.28	0.001±
HbA1c (%)	5.77±0.43	6.14±0.46	5.85±0.61	6.23±0.49	0.346#
C-peptide(ng/ml)	1.27±0.43	1.08±0.51	0.64±0.34	0.80±0.20	0.052#
*n (%)					
# One-Way ANOVA test, ± Kruskal Wallis test, ¶ Chi-Square test NGT; Fasting blood glucose <126 mg/dl and 2-hour blood glucose <140 mg/dl on an OGTT					
INDET; Fasting blood glucose <126 mg/dl and 2-hour blood glucose <140 mg/dl on an OGTT, but blood glucose at 60 minutes ≥200 mg/dl					
IGT; Fasting blood glucose <126 mg/dL and 2-hour blood glucose during OGTT 140–200 mg/dL					
CFRD without fasting hyperglycemia; Fasting blood glucose <126 mg/dL and 2-hour blood glucose during OGTT ≥200 mg/dL					
CFRD with fasting hyperglycemia; Fasting blood glucose ≥126 mg/dL (OGTT not required)					
Impaired fasting glucose (IFG); Fasting blood glucose 110–126 mg/dL, all blood glucose levels during the OGTT <200 mg/dL					

Of the 25 CF patients participating in the study, five (20%) were diagnosed with CFRD. Of the diabetic cases listed in Table 6, cases 1 and 2 were diagnosed using OGTT, case 3 using both an OGTT and HbA1c testing, and cases 4 and 5 using HbA1c testing alone. Cases 2 and 4 were diagnosed with diabetes at ages 8 and 7.4 years, respectively. Two (8%) of the five patients diagnosed with CFRD in our study were under the age of 10 at diagnosis. Delta-F508 homozygous mutation was detected in three of the five patients diagnosed with CFRD.

Table 6. Clinical, anthropometric, and laboratory characteristics of patients with diabetes					
	Case-1	**Case-2**	**Case-3**	**Case-4**	**Case-5**
Calendar age (years)	12,5	8	17	7,4	13
Age at diagnosis (months)	1	1	8	36	1
Gender	Female	Male	Male	Female	Kız
BW (kg)	33	20	50	24	23.5
BW sd	-2.01	-0.90	-2.35	-0.01	-4.96
Height (cm)	154	125.2	169	130	130.5

Table 6. Continued					
Height sd	-0.22	-0.33	-0.90	1.30	-4.55
BMI (kg/m^2)	13.9	13.3	17.5	14.2	13.8
BMI sd	-2.32	-2.12	-2.32	-0.95	-3.20
HbA1c (%)	5.9	6	6.8	6.8	6.6
Blood glucose level (mg/dL) 120 min into the OGTT	220	214	206	164	144
Total insülin	204	52	59	73	51
C-peptide (ng/ml)	0.83	0.59	1	1.35	0.5
Delta-508 homozygous mutation	-	+	+	-	+
OGTT, Oral Glucose Tolerance Test, BW: Body weight, BMI: Body mass index, SD: Standard deviation, HbA1c: Hemoglobin A1c					

Discussion

Cystic Fibrosis

A recently published meta-analysis and systematic review has reported that AGT associated with cystic fibrosis is the most common extrapulmonary comorbidity in CF patients, affecting one in three children with CF and one in two adults with CF (6). Of the 25 CF patients who participated in the study, AGT was detected in 13 (52%). The high occurrence of AGT that was observed in this study makes it a valuable starting point for raising awareness, helping to fill existing knowledge gaps in this area within our country and demonstrating that the prevalence of AGT associated with CF is higher than previously estimated. As CFRD is associated with microvascular complications that damage multiple organs, impaired lung function and increased mortality, the diagnosis and treatment of this condition at the earliest possible stage and age can help to delay its progression and maintain a better quality of life (9,10,16-18).

In the present study, 2 (8%) of the 5 (20%) patients diagnosed with CFRD were diagnosed before the age of ten. The diagnosis of these two patients, both under the age of ten, was made using HbA1c and an OGTT, with no fasting hyperglycaemia. Current guidelines advocate that the OGTT, which is the gold standard for diagnosing AGT, should only be performed from the age of ten onwards (11,12). The identification of CFRD in two patients under the age of ten in our study is of great significance, as it demonstrates that CFRD, the most severe subtype of CF associated with mortality and morbidity, can develop in patients under the age of ten. It has been reported that severe CFTR genotypes, including Delta-F508 homozygosity, increase the risk of CFRD and also elevate the risk of death (16). A notable finding in this study is that the delta-F508 homozygous mutation was detected in three of the five patients diagnosed with CFRD. There is a necessity for multicentre, prospective studies on CF gene mutations and the development of CFRD in children.

The development of IGT in CF children is primarily due to pancreatic beta-cell impairment, which results in insufficient insulin secretion. This impaired insulin response is an early sign of beta-cell dysfunction and is not typically related to autoimmune factors, as seen by the absence of islet cell antibodies in these patients (23). Impaired Glucose Tolerance (IGT) is a significant concern in children with CF, with prevalence rates typically ranging from 18% to as high as 39% in various studies (23,13). As stated in the relevant meta-analysis, the prevalence of IGT remains consistent over time and across age groups (6). In the present study, IGT was identified in 5 (20%) patients. This finding is consistent with the previously mentioned prevalence rates of IGT. The finding that the prevalence of IGT remains constant with age suggests that, in contrast to prevailing assumptions, prediabetes also occurs in early childhood. Moreover, recent findings indicate that IGT can manifest between the ages of 3 months and 5 years, thereby substantiating the notion of considering screening in younger children (13).

In cases of abnormal glucose tolerance, the presence of INDET is specific to CF. A study found that individuals classified as INDET on the OGTT were 10 times more likely to develop CFRD over a five-year period than those classified as IFG or NGT (24). In the present study, the investigation revealed the presence of INDET in five (20%) patients. A meta-analysis has indicated that, in a manner analogous to IGT, the prevalence of INDET remains constant over time or with age (6).

Nutritional status, including BMI and growth parameters, are critical in managing CF, as malnutrition can exacerbate the progression of CF-related complications, including diabetes (25). Insulin deficiency has been demonstrated to contribute to increased catabolism and a decrease in BMI, and typically manifests prior to a diagnosis of CFRD being made (5). Even mild glucose abnormalities, such as IGT, have been linked to

impaired nutrition and weight loss prior to the onset of overt CFRD (26). The present study revealed that the BW SD and BMI SD of CF patients diagnosed with AGT were significantly lower than those of patients diagnosed NGT. This finding suggests that CF patients, particularly those exhibiting signs of malnutrition and weight loss, should be screened for glucose abnormalities using an OGTT, alongside complications associated with other conditions.

Study Limitations

The present study is not without its limitations. The number of patients is insufficient to determine the prevalence of glucose abnormalities associated with CF. Due to the limited sample size, this study should be regarded as a preliminary observational study. However, as the study provides significant preliminary data on glucose abnormalities in children under the age of ten with CF in our country, it could serve as a starting point for multicentre studies to be conducted here. A further significant limitation is that the information available regarding patients' genetic test results for CFTR genotypes is limited and heterogeneous. CFTR genotype tests were conducted in the past and at different centres.

In conclusion, AGT affects one in two adults with CF and one in three children with CF; however, AGT is significantly underdiagnosed in children with CF. The results of the study demonstrated the presence of AGT in approximately half of the patient sample. The initial phases of CFRD tend to be asymptomatic; therefore, clinicians should adopt a proactive approach in conducting screening tests. Annual OGTT testing from the age of ten remains the gold standard for the diagnosis of CFRD. However, it is important to note that AGT frequently manifests prior to the age of ten. Despite the limited number of patients in this study, the findings support the hypothesis that screening for CFRD and AGT using an OGTT can be conducted from an early age. It is imperative that larger-scale, multicentre, prospective studies are conducted prior to the implementation of any amendments to the prevailing guidelines.

Conclusion

Contrary to popular belief, AGT can manifest in children with cystic fibrosis at an early age and is a relatively prevalent condition. The expansion of routine screening tests to encompass younger children in the future appears to be a viable proposition. AGT detected during this period has been shown to predict early progression to CFRD. Diagnosing CFRD at the earliest stage offers the opportunity to initiate early and appropriate intervention.

Ethical Approval: *Ethical approval was obtained from the Clinical Research Ethics Committee of University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital (approval no: 2011-KAEK-25 2021/11-15, date: November 3).*

Author Contributions:

Concept: H.A.A., Ö.K.
Literature Review: H.A.A., Ö.K.
Design: H.A.A., Ö.K.
Data acquisition: H.A.A., Ö.K.
Analysis and interpretation: H.A.A., Ö.K.
Writing manuscript: H.A.A.
Critical revision of manuscript: H.A.A., Ö.K.

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