

# Can HbA1c and 1-Hour Glucose Replace OGTT in Obese Children in Early Detection of Glucose Metabolism Disorders?

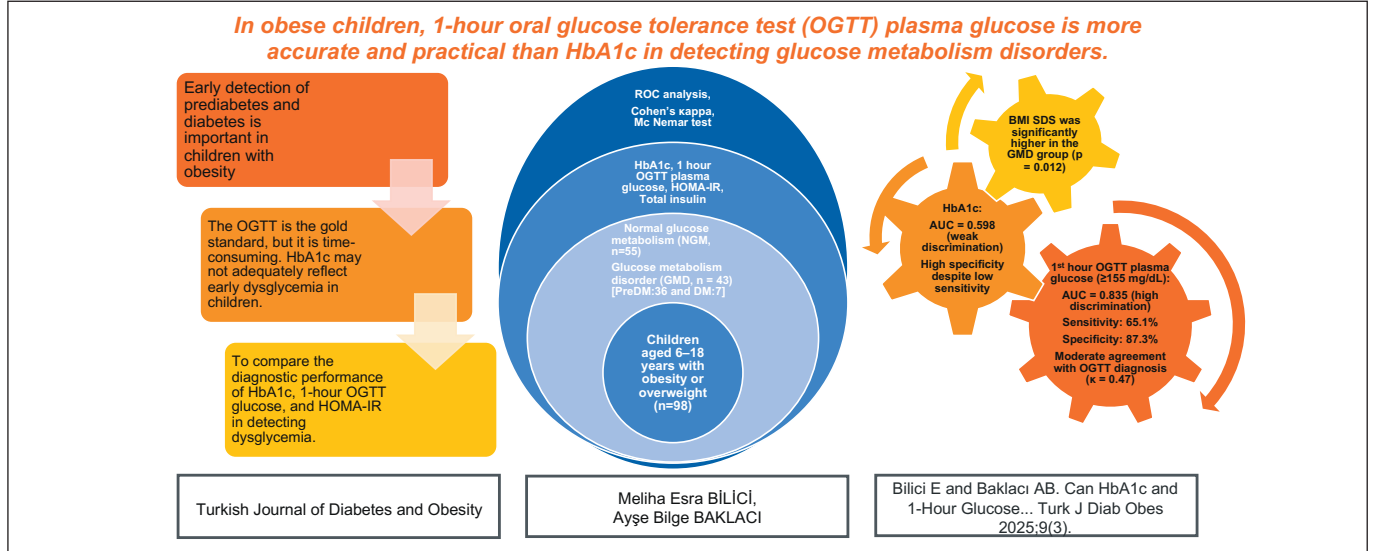
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## GRAPHICAL ABSTRACT



## ABSTRACT

**Aim:** This study aims to evaluate and compare the diagnostic performance of HbA1c and 1-hour plasma OGTT glucose levels for identifying glucose metabolism disorders (prediabetes or diabetes) in obese children and adolescents.

**Material and Methods:** Children aged 6–18 years with obesity who underwent OGTT between April 2021 and September 2025 were included, yielding a total of 98 cases in the study cohort. Participants were primarily categorized according to American Diabetes Association (ADA) criteria into two main groups: Normal glucose metabolism (NGM, n=55) and Glucose metabolism disorder (GMD, n=43), which included both prediabetes (n=36) and diabetes mellitus (n=7). Anthropometric and biochemical parameters were compared between groups using appropriate parametric or nonparametric tests. The diagnostic performance of HbA1c and 1-hour OGTT-PG ( $\geq 155$  mg/dL) for detecting GMD was evaluated using receiver operating characteristic (ROC) curve analysis, sensitivity, specificity, and agreement (Cohen's kappa) with the OGTT-based diagnosis..

**Results:** BMI SDS was significantly higher in the GMD group compared to the NGM group ( $2.6 \pm 1.5$  vs.  $2.1 \pm 1.4$ ,  $p = 0.012$ ). The 1-hour OGTT-PG level showed excellent discriminative ability for identifying GMD (AUC = 0.835,  $p < 0.001$ ), with a sensitivity of 65.1% and specificity of 87.3% at the  $\geq 155$  mg/dL cut-off. In contrast, HbA1c demonstrated weak discriminative ability for GMD (AUC

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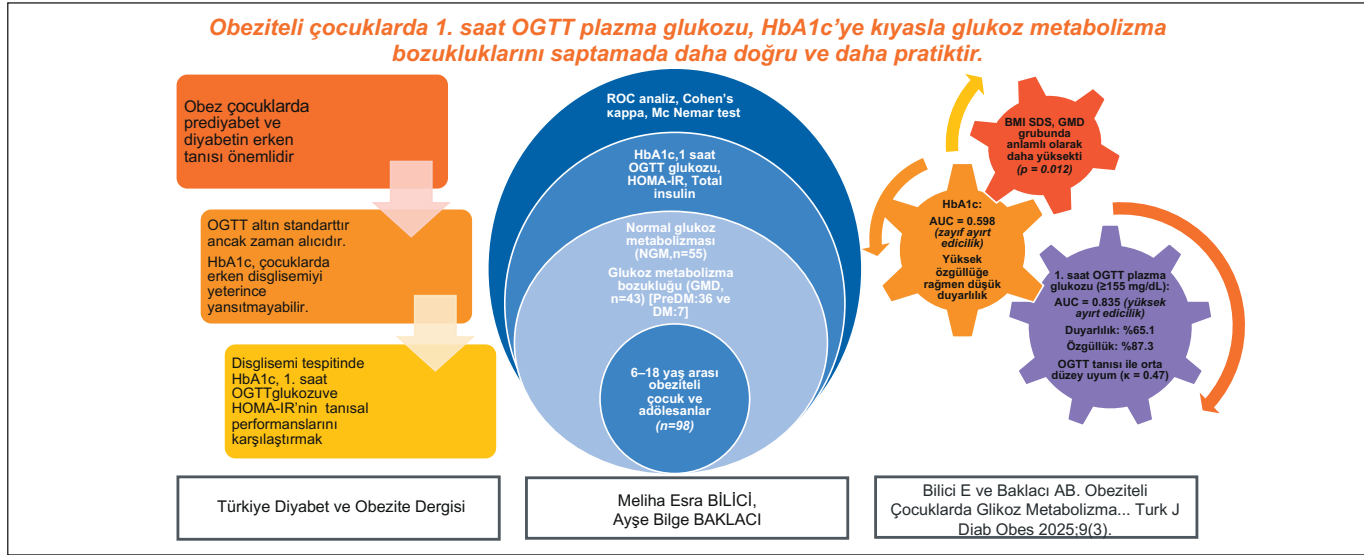
= 0.598,  $p = 0.080$ ). Agreement between 1-hour OGTT-PG and OGTT-based diagnosis was moderate ( $\kappa = 0.47$ ,  $p < 0.001$ ), whereas HbA1c alone did not show statistically significant concordance ( $\kappa = 0.136$ ,  $p = 0.146$ ).

**Conclusion:** In children with obesity, the 1-hour OGTT-PG level is a more sensitive and accurate marker for identifying glucose metabolism disorders than HbA1c. Incorporating the 1-hour OGTT-PG measurement into the assessment of high-risk pediatric populations may facilitate the earlier detection of dysglycemia.

**Keywords:** HbA1c, 1-hour OGTT-PG, OGTT, Prediabetes, Pediatric obesity, ROC analysis

## Obeziteli Çocuklarda Glikoz Metabolizma Bozukluklarının Erken Tespitinde HbA1c ve 1. Saat OGTT Plazma Glukoz Düzeyi OGTT'nin Yerini Alabilir mi?

### GRAFİKSEL ÖZET



### ÖZ

**Amaç:** Bu çalışmanın amacı, obeziteli çocuk ve ergenlerde glukoz metabolizma bozukluğunu (prediyabet veya diyabet) belirlemede HbA1c ve 1. Saat OGTT glukoz düzeylerinin tanasal performansını değerlendirmek ve karşılaştırmaktır.

**Gereç ve Yöntemler:** Çalışmaya, Nisan 2021 ile Eylül 2025 tarihleri arasında OGTT yapılmış olan 6-18 yaş arası obeziteli çocuklar çalışmaya dahil edilmiş olup, çalışma grubu toplam 98 olgudan oluşmaktadır. Katılımcılar Amerikan Diyabet Birliği (ADA) kriterlerine göre Normal glukoz metabolizması grubu (NGM, n=55) ve prediyabet (n=36) ile diyabetes mellitusu (n=7) içeren Glukoz metabolizma bozukluğu grubu (GMB, n=43) olarak iki gruba ayrılmıştır. Antropometrik ve biyokimyasal parametreler gruplar arasında uygun parametrik veya nonparametrik testler kullanılarak karşılaştırılmıştır. HbA1c ve 1. Saat OGTT plazma glukozunun ( $\geq 155$  mg/dL) GMB'yi saptamadaki tanasal performansı, alıcı işletim karakteristiği (ROC) eğrisi analizi, duyarlılık, özgüllük ve OGTT'ye dayalı tanı ile uyum Cohen's kappa testi kullanılarak değerlendirilmiştir.

**Bulgular:** BMI SDS, GMB grubunda NGM grubuna kıyasla anlamlı derecede daha yüksekti ( $2,6 \pm 1,5$ 'ye karşı  $2,1 \pm 1,4$ ,  $p = 0,012$ ). 1. Saat OGTT plazma glukoz düzeyi, GMB'yi belirlemede mükemmel ayırt edici yetenek göstermiş ( $AUC = 0,835$ ,  $p < 0,001$ ),  $\geq 155$  mg/dL eşik değerinde %65,1 duyarlılık ve %87,3 özgüllük sağlamıştır. Buna karşılık, HbA1c GMB için zayıf bir ayırt edici yetenek göstermiştir ( $AUC = 0,598$ ,  $p = 0,080$ ). 1. saat OGTT plazma glukozu ile OGTT'ye dayalı tanı arasındaki uyum orta düzeydeyken ( $\kappa = 0,47$ ,  $p < 0,001$ ), HbA1c için istatistiksel olarak anlamlı bir uyum saptanmamıştır ( $\kappa = 0,136$ ,  $p = 0,146$ ).

**Sonuç:** Obez çocuklarda, 1. saat OGTT plazma glukoz düzeyi, HbA1c'ye kıyasla glukoz metabolizma bozukluklarını belirlemede daha duyarlı ve doğru bir belirteçtir. Yüksek riskli pediatrik popülasyonların değerlendirmesinde 1. saat glukoz ölçümünün dahil edilmesi, disgliseminin daha erken saptanmasını kolaylaştırabilir.

**Anahtar Sözcükler:** HbA1c, 1 saatlik OGTT glukozu, OGTT, Prediyabet, Çocukluk çağı obezitesi, ROC analizi

## INTRODUCTION

Childhood obesity has emerged as a major problem for global public health, significantly elevating the risk of acquiring type 2 diabetes mellitus (T2DM) and prediabetes in overweight and obese children. The resistance to insulin (IR), impaired glucose tolerance (IGT), impaired fasting glucose (IFG), and T2DM are the predominant anomalies in glucose metabolism identified in this population (1,2). These disturbances are influenced not only by obesity-related metabolic changes but also by the physiological insulin resistance that characterizes puberty (3).

Traditionally, glucose metabolism abnormalities have been diagnosed, and future diabetes risk has been predicted using fasting plasma glucose (FPG), 120-minute plasma glucose (2-hr-OGTT-PG) of the oral glucose tolerance test (OGTT), and glycated hemoglobin (HbA1c) (4–6). In recent years, HbA1c has gained attention as an alternative diagnostic tool due to its ability to reflect average blood sugar levels throughout the previous two to three months and its non-invasive, practical application (4–7). This recommendation is largely based on adult studies demonstrating strong associations between HbA1c, future diabetes development, and microvascular complications (8). However, in children, the diagnostic reliability of HbA1c is influenced by several factors, including pubertal stage, ethnicity, hemoglobin variants, and anemia (2,5).

Several studies have reported that HbA1c underestimates the prevalence of prediabetes compared with OGTT-based criteria and has limited sensitivity for detecting early glucose dysregulation (8,9). Similarly, multiple NHANES-based epidemiological studies have shown that HbA1c fails to identify a substantial proportion of individuals with OGTT-defined prediabetes (10,11). The American Diabetes Association (ADA) currently recommends the same HbA1c thresholds for children as for adults, defining prediabetes as 5.7–6.4% and diabetes as  $\geq 6.5\%$  (3). However, diagnostic performance in pediatric populations is highly variable, with reported sensitivity and specificity ranging from 60–85% and 50–90%, respectively, depending on cutoff values, age, ethnicity, and obesity severity (11–13). These findings indicate that HbA1c alone is insufficient for diagnosing prediabetes or T2DM and highlight the need for complementary measures such as OGTT, 1-hour OGTT-PG (1hr-OGTT-PG), or HOMA-IR (6–8,10,13). Additionally, HOMA-IR values may vary during puberty, suggesting the necessity for age- and sex-specific reference ranges (14).

These limitations have led to growing interest in novel parameters derived from OGTT. Recent studies suggest that early post-load responses, such as the 1-hour OGTT-PG and glucose peak time, provide valuable insight into  $\beta$ -cell

dysfunction and future diabetes risk. In adults, a 1-hour OGTT-PG level  $\geq 155$  mg/dL has been associated with a higher likelihood of developing diabetes and adverse cardiometabolic outcomes (15). Pediatric studies have shown similar trends, indicating that 1-hour OGTT-PG can detect postprandial abnormalities not captured by HbA1c or FPG (16), and that lower cutoff values (around 130 mg/dL) may improve sensitivity in children (12,13,15,17). Notably, the International Diabetes Federation (IDF) Position Statement has formally incorporated the 1-hour OGTT-PG value into its diagnostic framework, defining intermediate hyperglycemia (prediabetes) as a 1-hour OGTT-PG  $\geq 155$  mg/dL and suggesting that a level  $\geq 209$  mg/dL, if confirmed by a second test, can be diagnostic for diabetes following a 75-g OGTT (18). Although OGTT remains the gold standard for diagnosing glucose metabolism disorders in childhood obesity, its complexity and limited clinical applicability necessitate alternative parameters. However, reliance on HbA1c alone may lead to underdiagnosis, as evidenced by adult studies reporting a lower prevalence of diabetes when diagnosed by HbA1c compared to OGTT criteria (19). Therefore, this study aimed to evaluate the relationship between OGTT findings and HbA1c, Homeostasis model assessment of insulin resistance (HOMA-IR), and 1-hour OGTT-PG levels in obese children and adolescents, to determine their diagnostic performance for detecting glucose metabolism disorders (prediabetes or diabetes)

## MATERIALS and METHODS

### Study Population and Design

Overweight and obese children aged 6–18 years who underwent an OGTT to evaluate glucose metabolism at the Pediatric Endocrinology Clinic of Zonguldak Bulent Ecevit University between April 2021 and September 2025 were included in this cross-sectional study. Ethical approval for the study was obtained from the Zonguldak Bulent Ecevit University Clinical Research Ethics Committee, and the study was conducted in compliance with the principles of the Declaration of Helsinki (approval No. 2025/17). Written informed consent for the OGTT procedure was provided by all parents or legal guardians.

Participants were categorized according to their BMI, which was transformed into standard deviation scores (SDS) that were relevant to their age and sex. According to national BMI reference standards for Turkish children, a BMI SDS of  $\geq 1$  (corresponding to the 85th percentile) was used to define overweight, whereas a BMI SDS of  $\geq 2$  (corresponding to the 95th percentile) was used to define obesity (20). Patients with syndromic or hypothalamic obesity, those receiving diabetes treatment, or those using medications that could affect metabolism were excluded.

### Clinical and Biochemical Assessments

Detailed anthropometric assessments—including height, weight, and BMI SDS—were performed by trained clinicians using standardized techniques at admission. Standardized anthropometric evaluations were performed by trained personnel. A Harpenden stadiometer was used to measure standing height to the closest 0.1 cm, and a calibrated digital scale was used to assess body weight. The middle point between the iliac crest and the lower costal border was used to measure the waist circumference. All anthropometric measurements were converted to age- and sex-specific SDS using national reference growth curves (20) via the ChildMetrics online calculator (<https://childmetrics.com>). Laboratory analyses included fasting plasma glucose, HbA1c, fasting insulin; lipid profile components—high-density cholesterol (HDL-C), triglycerides, and low-density lipoprotein cholesterol (LDL-C)—liver enzymes, including alanine and aspartate aminotransferase (ALT and AST), as well as thyroid stimulating hormone (TSH) and free thyroxine levels (FT4) were noted. Routine biochemical measurements were performed using spectrophotometric methods on an automated analyzer. Serum insulin, TSH, and FT4 concentrations were determined by electrochemiluminescence immunoassay (Cobas 6000, Roche Diagnostics, Mannheim, Germany). HbA1c levels were measured using high-performance liquid chromatography (Lifotronic H9 Hemoglobin Analyzer). Insulin resistance was assessed with the HOMA-IR index, which was calculated as the product of fasting insulin ( $\mu\text{U/mL}$ ) and FPG ( $\text{mg/dL}$ ), divided by 405.

### Oral Glucose Tolerance Test (OGTT) and Diagnostic Grouping

The stimulated test was administered following a minimum of three days of unrestricted carbohydrate intake and an overnight fast of approximately 10 hours. Participants received an oral glucose load at a dose of 1.75 g/kg (max 75 g), under medical supervision. Venous blood samples were obtained to determine plasma glucose and insulin concentrations at 0, 30, 60, 90, and 120 minutes following the glucose consumption. The American Diabetes Association's diagnostic criteria were used to interpret test results (4).

As the primary analysis strategy, participants were first categorized into two main groups: the Normal glucose metabolism group (NGM) and the Glucose metabolism disorder group (GMD). NGM was defined as FPG  $<100$  mg/dL and 2-hr-OGTT-PG  $<140$  mg/dL. The glucose metabolism disorder group included individuals with either prediabetes or type 2 diabetes mellitus. Prediabetes was defined as FPG 100–125 mg/dL and/or 2-hr-OGTT-PG 140–199 mg/dL, while T2DM was defined as FPG

$\geq 126$  mg/dL and/or 2-hr-OGTT-PG  $\geq 200$  mg/dL (3). For secondary and descriptive purposes, with a focus on the prediabetes group, participants were subdivided into three subgroups: NGM, prediabetes, and T2DM. However, due to the very small sample size of the T2DM subgroup, no statistical comparisons were performed across the three subgroups (NGM, prediabetes, T2DM). Therefore, the two-group categorization (NGM vs. GMD) formed the basis for all primary analyses. A secondary exploratory analysis was conducted specifically comparing the NGM group to the prediabetes subgroup. Data for the T2DM group are presented descriptively. An OGTT plasma glucose threshold of  $\geq 155$  mg/dL was employed for one hour (4). HbA1c levels were categorized as  $<5.7\%$ ,  $5.7\text{--}6.4\%$ , and  $\geq 6.5\%$  according to ADA recommendations (4).

### Statistical Analysis

International Business Machines Corporation Statistical Package for the Social Sciences (IBM SPSS) Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. The Shapiro-Wilk test was used to analyze the distribution of the data. Non-normally distributed data were reported as median (minimum–maximum), whereas variables with a normal distribution were summarized as mean  $\pm$  standard deviation. The Mann-Whitney U test was utilized for nonparametric data, and the Independent Samples t-test for normally distributed variables when comparing two groups. The diagnostic utility of HbA1c and 1-hour OGTT-PG for identifying glucose metabolism disorders was evaluated. Their discriminative capacity was assessed using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) with 95% confidence intervals (CI) was computed. For pertinent HbA1c and 1-hour OGTT-PG thresholds, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for identifying OGTT-defined GMD were reported.

The agreement between diagnostic classifications based on standard OGTT criteria, HbA1c thresholds, and the 1-hour OGTT-PG cut-off ( $\geq 155$  mg/dL) was evaluated using cross-tabulation, Cohen's kappa coefficient, and McNemar's test.

Correlations between continuous, non-normally distributed parameters were analyzed using Spearman's rank correlation coefficient. Trends across ordered HbA1c categories (normal, prediabetes range) were assessed using the linear-by-linear association test.

All analyses were deemed statistically significant if the two-tailed p-value was less than 0.05.

A post-hoc power analysis was performed using G-Power 3.1 for the primary comparison of this study (NGM vs. GMD) utilizing the reported large effect size (Cohen's  $d = 1.07$ ) for the 1-hour OGTT-PG level. With the current sample sizes (NGM:  $n=55$ , GMD:  $n=43$ ) and a significance level of  $\alpha=0.05$ , the analysis indicated a statistical power exceeding 99%, confirming that the study was adequately powered to detect this clinically significant difference.

## RESULTS

A total of 98 children were included in the analysis; the average age was  $12.8 \pm 2.8$  years, and just over half of the participants were female (54%). Among them, 56% had normal glucose metabolism (NGM,  $n = 55$ ), while 42% ( $n = 37$  prediabetes,  $n = 7$  diabetes) were classified as having GMD. Sex distribution did not differ significantly between the groups ( $p = 0.757$ ). TA summary of the anthropometric and biochemical features of the study population is provided in Table 1.

### Anthropometric and Biochemical Characteristics

Overall anthropometric measures were comparable between the normal glucose metabolism and glucose metabolism

disorder groups; however, indices related to adiposity were higher among participants with glucose metabolism disorder, including body mass index and body mass index standard deviation score ( $p = 0.007$  and  $p = 0.012$ , respectively).

With respect to laboratory findings, markers of glycemic control and insulin secretion, as well as alanine aminotransferase levels, showed significant between-group differences, as detailed in Table 1.

### Diagnostic Parameter Analysis

Paired diagnostic analysis evaluated the performance of HbA1c, HOMA-IR, and 1-hour OGTT-PG in predicting GMD. Only the 1-hour OGTT-PG ( $p < 0.001$ ) and fasting insulin ( $p = 0.007$ ) levels were significantly higher in the GMD group compared with the NGM group, while no differences were observed in HbA1c or HOMA-IR.

Table 2 presents a comparison of HbA1c, 1-hour OGTT-PG, total insulin, and HOMA-IR values among the NGM and GMD groups. Cases with GMD had significantly higher 1-hour OGTT-PG levels compared to those with normal glucose metabolism ( $173.7 \pm 53.5$  mg/dL vs.  $129.5 \pm 26.2$  mg/dL,  $p < 0.001$ ). Total insulin secretion during the OGTT

**Table 1:** Anthropometric and Biochemical Characteristics of the Study Population

Anthropometric Parameters (mean $\pm$ SD)	Study Group (n=98)	Normal Glucose Metabolism (n=55)	Glucose Metabolism Disorder (n=43)			p-value
			Total GMD	Pre DM(n:36)	DM(n:7)	
Age (years)	$12.8 \pm 2.8$	$12.9 \pm 3$	$12.8 \pm 2.5$	$12.8 \pm 2.6$	$13.1 \pm 2.6$	0,994
Body weight (BW) (kg)	$79.5 \pm 30.3$	$82.6 \pm 31.1$	$75.6 \pm 29.1$	$71.8 \pm 24.2$	$94.8 \pm 44.4$	0.144
BW SDS	$2.7 \pm 1.9$	$3.0 \pm 2.0$	$2.3 \pm 1.8$	$2.1 \pm 1.7$	$3.4 \pm 1.8$	0.149
Height (cm)	$158.1 \pm 16.7$	$158.1 \pm 18.1$	$158.1 \pm 14.9$	$157.3 \pm 15.3$	$162.3 \pm 12.5$	0.996
Height SDS	$0.5 \pm 1.2$	$0.6 \pm 1.2$	$0.5 \pm 1.2$	$0.4 \pm 1.2$	$0.8 \pm 0.8$	0.894
BMI (kg/m <sup>2</sup> )	$30.7 \pm 8.8$	$31.9 \pm 9.2$	$29.1 \pm 8.1$	$28.1 \pm 6.8$	$34.5 \pm 12.2$	<b>0.007</b>
BMI SDS	$2.4 \pm 1.5$	$2.6 \pm 1.5$	$2.1 \pm 1.4$	$2.0 \pm 1.3$	$2.7 \pm 1.5$	<b>0.012</b>
<b>Biochemical Parameters</b>						
AST (U/L)	$26.8 \pm 15.4$	$26.2 \pm 14.7$	$27.6 \pm 16.4$	$27.7 \pm 17.1$	$26.9 \pm 13.3$	0.373
ALT (U/L)	$32.0 \pm 25.9$	$29.9 \pm 18.9$	$34.6 \pm 32.7$	$32.3 \pm 31.1$	$46.0 \pm 40.7$	<b>0.027</b>
TSH ( $\mu$ IU/mL)	$3.2 \pm 2.4$	$3.3 \pm 2.9$	$3.1 \pm 1.5$	$3.1 \pm 1.5$	$3.1 \pm 1.2$	0.655
Free T4 (ng/dL)	$1.04 \pm 0.40$	$1.0 \pm 0.4$	$1.05 \pm 0.30$	$1.0 \pm 0.3$	$1.1 \pm 0.3$	0.649
Total Cholesterol (mg/dL)	$161.3 \pm 33.2$	$160.3 \pm 34.5$	$162.6 \pm 31.7$	$158.7 \pm 31.2$	$179.3 \pm 30.7$	0.742
Triglycerides (mg/dL)	$123.2 \pm 54.9$	$122.2 \pm 55.8$	$124.8 \pm 54.3$	$117.9 \pm 48.6$	$154.6 \pm 71.0$	0.835
HDL (mg/dL)	$43.8 \pm 9.4$	$45.4 \pm 10$	$41.6 \pm 8.2$	$42.2 \pm 8.5$	$39.4 \pm 7.3$	0.598
LDL (mg/dL)	$92.4 \pm 27.6$	$90.5 \pm 28.8$	$95.3 \pm 26$	$92.1 \pm 25.9$	$109.0 \pm 23.7$	0.523

Data are expressed as mean  $\pm$  standard deviation.

The p-value represents the comparison between the Normal Glucose Metabolism (NGM) and the combined Glucose Metabolism Disorder (GMD) groups, performed using the Independent Samples t-test or the Mann-Whitney U test, as appropriate for the distribution of the data. Data for the prediabetes and diabetes subgroups are presented for descriptive purposes only and were not included in the statistical comparison.

**BMI**, body mass index; **SDS**, standard deviation score; **HDL-C**, high-density lipoprotein cholesterol; **LDL-C**, low-density lipoprotein cholesterol; **HOMA-IR**, homeostasis model assessment of insulin resistance; **FPG**, fasting plasma glucose; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **TSH**, thyroid-stimulating hormone; **DM**, diabetes mellitus.

was also higher in the GMD group, although this difference did not reach statistical significance (median 669.2 vs. 531  $\mu\text{U/mL}$ ,  $p = 0.357$ ). No significant differences were found between the NGM and GMD groups regarding HbA1c values ( $5.7 \pm 0.62\%$  vs.  $5.56 \pm 0.51\%$ ,  $p = 0.062$ ) or HOMA-IR values (median 9.4 vs. 7.1,  $p = 0.697$ ). In the NGM group, HbA1c was between 5.7–6.5% in 23% of cases, and  $\geq 6.5\%$  in two cases. In the GMD group, 16 prediabetes and one diabetes patient had false-negative HbA1c values.

### Diagnostic Performance of 1-hour OGTT- PG and HbA1c for GMD

The diagnostic performance of the 1-hour OGTT-PG and HbA1c for identifying glucose metabolism disorders (prediabetes or T2DM) is detailed in Table 3. The 1-hour plasma OGTT glucose demonstrated excellent discriminative ability,

with an AUC of 0.835 (95% CI: 0.758–0.913,  $p < 0.001$ ). Applying the literature-based cut-off of  $\geq 155$  mg/dL yielded a sensitivity of 65.1% and a specificity of 87.3% for detecting GMD. HbA1c showed weaker performance for identifying GMD, with an AUC of 0.598 (95% CI: 0.488–0.708,  $p = 0.080$ ). The standard diagnostic cut-off of  $\geq 6.5\%$  had a very high specificity (96.3%) but a low sensitivity (16.3%) for detecting dysglycemia in this cohort.

### OGTT 1-hour Plasma Glucose Cut-Off Analysis

When OGTT was used as the reference standard for diabetes diagnosis, a 1-hour OGTT-PG threshold of  $\geq 180$  mg/dL demonstrated excellent discriminative power (AUC = 0.965; 95% CI: 0.925–1.000;  $p < 0.001$ ). However, coordinate analysis revealed that values exceeding 180 mg/dL were associated with a marked decline in specificity, making this a

**Table 2:** Comparison of HbA1c, 1-hour OGTT-PG, and insulin parameters among normal glucose metabolism (NGM) and prediabetes, diabetes subgroups

Variable	NGM (n=55)	Glucose Metabolism Disorder (n=43)			p-value
		Total	Prediabetes (n=36)	Diabetes (n=7)	
HbA1c (%)	5.56 $\pm$ 0.51	5.7 $\pm$ 0.62	5.65 $\pm$ 0.56	6.30 $\pm$ 0.70	0.062 *
HOMA-IR	7.1 (1,5-14)	9.4 (2.6-78)	9.4 (2.6-78)	9.4 (4.4-19.2)	0.697**
1-hr glucose (mg/dL)	129.5 $\pm$ 26.2	173.7 $\pm$ 53.5	160.6 $\pm$ 42.1	246.6 $\pm$ 48.7	<0.001*
Total insulin ( $\mu\text{U/mL}$ )	531 (64-1171)	669.2 (87.6-2255.8)	669.8 (87.6-2255.8)	664 (298-1164)	0.357**
FPG (mg/dL)	92.9 $\pm$ 7.7	100.2 $\pm$ 11.6	99.3 $\pm$ 10.7	104.6 $\pm$ 15.9	<0.001
Fasting Insulin ( $\mu\text{U/mL}$ )	27.3 $\pm$ 15.7	29.8 $\pm$ 21.2	27.8 $\pm$ 19.3	40.0 $\pm$ 28.8	0.007

Data are presented as mean  $\pm$  standard deviation for normally distributed variables and as median (minimum–maximum) for non-normally distributed variables.

The p-value represents the comparison between the Normal Glucose Metabolism (NGM) and the combined Glucose Metabolism Disorder (GMD) groups. Data for the prediabetes and diabetes subgroups are presented for descriptive purposes only and were not included in the statistical comparison.

\*Comparison performed using Independent Samples t-test. \*\*Comparison performed using Mann-Whitney U test.

NGM, normal glucose metabolism; GMD, glucose metabolism disorder.

**Table 3:** Diagnostic performance of 1-hour OGTT-PG and HbA1c for predicting glucose metabolism disorders

Parameter	Cut-off	AUC (95% CI)	Sensitivity (%)	Specificity (%)	p-value
<b>For Identifying Glucose Metabolism Disorder (GMD)</b>					
1-hour OGTT-PG	155 mg/dL (literature)	0.835 (0.758–0.913)	65.1	87.3	<0.001
	140,1 mg/dL (optimal)	0.762 (0.684–0.895)	68	73.7	<0.001
HbA1c	5.85% (optimal)	0.598 (0.488–0.708)	34.9	83.6	0.080
	$\geq 6.5\%$ (diagnostic)	0.588 (0.468–0.708)	16.3	96.4	0.153
<b>For Identifying Prediabetes (Secondary Analysis)</b>					
1-hour OGTT-PG	155 mg/dL (literature)	0.732 (0.628–0.836)	62.8	87.3	<0.001
HbA1c	5.85% (optimal)	0.548 (0.431–0.665)	30.6	81.8	0.437

The primary analysis evaluates the ability to identify glucose metabolism disorders (GMD). A secondary analysis focusing solely on prediabetes is also presented. Due to the small sample size of the diabetes subgroup (n=7), a separate ROC analysis for diabetes alone was not performed.

ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; GMD, glucose metabolism disorder (prediabetes + diabetes). Agreement Statistics (for GMD diagnosis): Cohen's  $\kappa$  between 1-hour OGTT-PG ( $\geq 155$  mg/dL) and OGTT-based diagnosis: 0.47,  $p < 0.001$ .

McNemar's test:  $p = 0.230$ .

highly specific but low-sensitivity criterion best suited for confirming rather than screening for diabetes.

For a more balanced approach, thresholds in the 160–170 mg/dL range maintained a more favorable profile, with high sensitivity and acceptable specificity. In fact, the Youden Index identified 160.4 mg/dL as the statistically optimal cut-off for maximizing overall diagnostic accuracy. In our cohort, the literature-based cut-off of  $\geq 155$  mg/dL identified dysglycemia effectively: it was present in 16.4% of NGM subjects, 55.6% of those with prediabetes, and 100% of diabetes cases ( $p < 0.001$ ), overall corresponding to 36.7% of the entire cohort.

Separate ROC analysis for detecting any dysglycemia (NGM vs. GMD) identified 117 mg/dL as the point closest to the top-left corner of the ROC curve, providing the highest sensitivity (83.7%) among balanced points, albeit with moderate specificity (63.6%) (AUC = 0.762; 95% CI: 0.660–0.864;  $p < 0.001$ ) (Table 2). For practical clinical purposes, however, a cut-off level of 140 mg/dL offers a more balanced sensitivity (68%) and specificity (73.9%) for initial risk stratification (AUC: 0.776, 95% CI: (0.684–0.895);  $p < 0.001$ ).

### Agreement Analyses

When OGTT was used as the reference standard for identifying diabetes in our cohort, HbA1c  $\geq 6.5\%$  had 71.4% sensitivity and 96.3% specificity, with positive and negative predictive values of 62.5% and 97.5%, respectively. McNemar's test showed no significant discordance ( $p = 0.3100$ ), while Cohen's  $\kappa = 0.68$  indicated moderate agreement. It should be noted that these performance metrics are derived from a small number of diabetes cases ( $n=7$ ) and should be interpreted with caution. Cross-tabulation revealed that elevated 1-hour OGTT-PG occurred in 27.5% of cases with normal HbA1c, 43.2% with HbA1c 5.7–6.5%, and 80% with HbA1c  $\geq 6.5\%$  ( $p = 0.047$ ). Spearman correlation confirmed a modest association between HbA1c category and 1-hour OGTT-PG ( $\rho = 0.234$ ,  $p = 0.027$ ), whereas Cohen's  $\kappa = 0.136$  indicated slight agreement.

Overall, the 1-hour OGTT-PG demonstrated the best discriminative ability for detecting dysglycemia in children in this study. Although HbA1c showed high specificity at the diagnostic threshold in our sample, its sensitivity remained limited, supporting the use of combined assessment in pediatric populations.

### DISCUSSION

We compared HbA1c, 1-hour OGTT-PG, total insulin, and HOMA-IR levels between children with NGM and those with glucose metabolism disorders in the present study. Our findings indicate that the 1-hour OGTT-PG level is a par-

ticularly strong parameter for distinguishing glucose metabolism disorders in children, whereas HbA1c shows limited sensitivity, especially in detecting prediabetes. Current diagnostic approaches and ADA-recommended thresholds may yield different results depending on whether glucose-based or HbA1c-based criteria are used (1,11,16). Consistent with our findings, accumulating evidence suggests that the 1-hour plasma glucose level during OGTT is a reproducible and clinically informative marker that reflects early impairments in glucose homeostasis and  $\beta$ -cell function, and may identify individuals at increased cardiometabolic risk even when conventional diagnostic thresholds are not met (21–24). Such variability underscores the need to refine diagnostic strategies to avoid delayed identification of at-risk individuals during the prediabetic stage, which may result in missed opportunities for early intervention while  $\beta$ -cell function is still preserved (25,26). Therefore, there is a need for more sensitive diagnostic tools. Our study identifies the 1-hour OGTT-PG as a strong candidate to fill this gap, demonstrating superior discriminative ability compared to HbA1c for identifying glucose metabolism disorders in obese children.

Several large-scale studies have demonstrated that post-load glucose levels at the 1-hour time point  $\geq 155$  mg/dL is a better predictor of future T2DM and its related complications, particularly retinopathy, compared with fasting or post-load glucose levels at the 2-hour time point measurements (1,2,5,15,27). In our study, the performance of HbA1c for identifying glucose metabolism disorders (prediabetes or diabetes) was limited. The high specificity of HbA1c suggests it is reliable for confirming dysglycemia, whereas its low sensitivity limits its utility in early detection. Similar findings have been reported in other pediatric populations, highlighting the limitations of HbA1c for detecting prediabetes. Nowicka et al. reported sensitivity of 30–40% and specificity of over 90% for HbA1c at 6.5% in obese adolescents (8). Lee et al. also demonstrated that HbA1c  $\geq 6.5\%$  had low sensitivity ( $\sim 32\%$ ) but high specificity (98%) compared to OGTT for T2DM diagnosis (24). Our findings align with this pattern, showing that HbA1c had weak discriminative ability for identifying prediabetes in children. Pediatric HbA1c performance is generally lower than in adults, and physiological insulin resistance and transient glucose elevations during puberty may partially explain this difference (28). Additionally, HbA1c reflects not only average glycemia but also erythrocyte lifespan and hemoglobin structure, making it susceptible to influences such as iron deficiency anemia, hemoglobinopathies (e.g., thalassemia, sickle cell disease), and ethnicity (29,30). Iron deficiency prolongs erythrocyte lifespan, leading to higher measured HbA1c, whereas hemolytic anemia or certain hemoglobin variants

can falsely lower HbA1c. Furthermore, African-American, Asian, and Hispanic populations exhibit higher HbA1c levels than whites at comparable glycemia (24,30). These factors suggest that HbA1c alone may be insufficient for early detection of glucose metabolism disorders in children or individuals from diverse ethnic backgrounds. Moreover, current guidelines emphasize that HbA1c is more suitable for confirming established dysglycemia rather than for early detection in pediatric populations (31,32). Therefore, combining HbA1c with OGTT may improve diagnostic accuracy in obese and high-risk populations. In our study, the AUC of HbA1c for detecting prediabetes was 0.548 and not statistically significant ( $p=0.437$ ), indicating limited performance for early glucose abnormalities. In contrast to HbA1c, the 1-hour OGTT-PG demonstrated good discriminative ability for identifying glucose metabolism disorders in our study. This supports 1-hour OGTT-PG as a stronger parameter than HbA1c for prediabetes detection. Similarly, Brar et al. reported an AUC of 0.852 for 1-hour OGTT-PG, highlighting its high discriminative power (22). Multiple studies have also shown that 1-hour OGTT-PG  $>155$  mg/dL is a strong predictor of future glucose intolerance and T2DM (33,34). This association is also evident in Turkish pediatric populations. In obese children with normal glucose tolerance, an elevated 1-hour OGTT-PG level ( $\geq 155$  mg/dL) was associated with a worse metabolic profile, including higher insulin resistance and a greater frequency of non-alcoholic fatty liver disease, marking it as an early risk indicator (35). Furthermore, in obese Turkish children, a 1-hour OGTT-PG level  $\geq 155$  mg/dL was linked to a significantly higher risk of concurrent impaired glucose tolerance, underscoring its immediate diagnostic relevance (16).

Although OGTT has long been the standard method for assessing glucose metabolism disorders, current WHO and ADA criteria do not include 1-hour OGTT-PG in the diagnostic process. Historically, 1-hour OGTT-PG has been recognized as an important marker for early-stage diabetes. Recent evidence further suggests that 1-hour OGTT-PG reflects not only impaired glucose tolerance but also early insulin resistance and  $\beta$ -cell dysfunction, making it a comprehensive early indicator of dysglycemia. Therefore, including 1-hour OGTT-PG in diagnostic algorithms could provide clinical benefit, particularly in high-risk pediatric populations.

The superior ability of 1-hour OGTT-PG to detect early abnormalities compared with HbA1c may be explained by postprandial glucose rises reflecting first-phase insulin secretion defects, whereas HbA1c represents average glycemia and cannot capture short-term glucose excursions (28,36). In our cohort, a positive correlation was observed

between HbA1c categories and 1-hour OGTT-PG (Spearman's  $\rho=0.234$ ,  $p=0.027$ ), but agreement was low ( $\kappa=0.136$ ), suggesting that these tests reflect different stages of glucose dysregulation and may be used complementarily.

The optimal 1-hour OGTT-PG cutoff for identifying prediabetes was 117 mg/dL, with a sensitivity of 83.7% and specificity of 63.6%. in our study. This lower threshold appears to identify early dysglycemia more effectively than the traditional 155 mg/dL cutoff, albeit at the expense of lower specificity. Despite a limited sample size, 1-hour OGTT-PG  $>180$  mg/dL showed potential to identify diabetes cases with high accuracy (AUC 0.9). For example, Park et al. reported that a 1-hour OGTT-PG between 155–199 mg/dL could serve as a recommended threshold for prediabetes (23). In a cohort of 1,250 non-diabetic Asian cases, a 1-hour OGTT-PG cutoff of 10.7 mmol/L (192.6 mg/dL) predicted T2DM development over three years with similar effectiveness to 2-hour OGTT, while also reflecting  $\beta$ -cell function (24). Longitudinal studies indicate that a 1-hour OGTT-PG level predicts retinopathy risk as effectively as a 120-minute plasma glucose level and provides a shorter, cost-effective, and practical alternative (37). Collectively, these findings highlight the clinical potential of 1-hour OGTT-PG as a sensitive, feasible, and cost-effective marker for early identification of glucose dysregulation in children.

Interpretation of the findings should take into account certain methodological constraints. First, the modest sample size and the single-center design may limit generalizability. Second, the small number of participants with diabetes ( $n=7$ ) precluded a robust separate analysis of this subgroup; therefore, our primary analyses and conclusions focus on the detection of glucose metabolism disorders as a combined entity and on the prediabetes stage. Third, the study's cross-sectional design precludes evaluation of long-term outcomes, such as progression from prediabetes to diabetes. Fourth, potential confounding factors affecting HbA1c levels, including iron deficiency anemia or hemoglobin variants, were not systematically assessed. In addition, pubertal stage and ethnic variations—both of which can influence glucose metabolism and HbA1c interpretation—were not analyzed in detail. Finally, the study did not include a randomized controlled design, which would be required to establish causal inferences and to compare diagnostic strategies more robustly. Despite these limitations, our study provides valuable evidence supporting the role of 1-hour OGTT-PG as a practical and sensitive indicator for detecting early glucose dysregulation in obese children and adolescents.

In conclusion, our data support that the 1-hour OGTT-PG level during OGTT provides a more sensitive indicator of early glucose dysregulation in obese children and adoles-

cents than HbA1c. While HbA1c  $\geq 6.5\%$  maintains high specificity, its low sensitivity limits its role as a standalone diagnostic marker, particularly in detecting prediabetes. Incorporating 1-hour OGTT-PG measurements into OGTT interpretation may improve the identification of children at risk for diabetes and facilitate earlier interventions before irreversible  $\beta$ -cell dysfunction occurs. Overall, the 1-hour OGTT-PG appears to be a valuable biomarker for pediatric glucose metabolism disorders, yet it should be interpreted together with HbA1c, 2-hour glucose values, and relevant clinical risk factors. Future large-scale, longitudinal studies are needed to validate the diagnostic and predictive value of 1-hour OGTT-PG levels in pediatric populations. Specifically, research including a sufficient number of children with type 2 diabetes is warranted to explore the utility of this parameter across the full spectrum of glucose metabolism disorders, from prediabetes to established diabetes. Such studies could determine whether the 1-hour OGTT-PG offers a practical, cost-effective, and less burdensome tool for screening and monitoring in high-risk pediatric populations

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#### Author's Contributions

**Meliha Esra Bilici** conceived and designed the study, coordinated and supervised data collection, interpreted the results, and wrote the manuscript. **Ayşe Bilge Baklaci** contributed to patient evaluation and data collection and provided input during manuscript revision. All authors reviewed and approved the final version of the manuscript.

#### Conflict of Interest

The authors declare that they have no conflict of interest.

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#### Ethical Approval

This study was approved by the Zonguldak Bulent Ecevit University Clinic Research Ethics Committee and adhered to the ethical standards of the Declaration of Helsinki (approval date: October 1, 2025; approval number: 2025/17). Informed Consent: Due to the retrospective nature of the study, the institutional committee waived the need for obtaining informed consent.

#### Peer Review Process

Extremely and externally peer-reviewed.

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