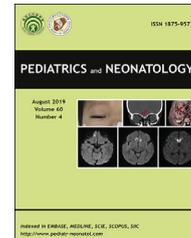




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Original Article

Comparison of HbA1c and OGTT for the diagnosis of type 2 diabetes in children at risk of diabetes

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Keywords

Diabetes mellitus;
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Glucosuria

Background: The aim of this study was to evaluate the correlation between plasma glucose and HbA1c and the diagnostic accuracy of HbA1c as a screening tool to identify asymptomatic diabetes mellitus in children and adolescents with obesity or asymptomatic glucosuria.

Methods: A total of 190 subjects who underwent an oral glucose tolerance test (OGTT) to confirm diabetes were categorized into normal glucose tolerance (NGT; n = 117), impaired glucose tolerance (IGT; n = 33), and diabetes (DM; n = 40) according to the OGTT. Forty-seven patients with DM were diagnosed by either OGTT or HbA1c levels. The diagnostic accuracy for the detection of diabetes is based on 47 patients. Laboratory tests were performed after 12 h of fasting.

Results: According to the HbA1c criterion, 107 (55.3%) subjects were in the NGT group, 41 (21.6%) were in the IGT group, and 42 (22.1%) were in the DM group. Diagnostic sensitivities of HbA1c and 2-hour plasma glucose level following OGTT (2-h OGTT) for DM were significantly higher than that of fasting plasma glucose, FPG (89.4, 85.1 vs. 63.8%). In addition, the area under the curves of diagnostic criteria was 0.970 for HbA1c, 0.939 for FPG and 0.977 for 2-h OGTT. Mean FPG and 2-h OGTT for HbA1c level >6.5% were 115.2 mg/dL and 181.8 mg/dL, respectively. The optimal HbA1c level cut-off point for predicting DM is 6.15%, with a sensitivity of 95.7% in Korean children and adolescents.

Conclusion: The HbA1c criterion $\geq 6.5\%$ was adequate to detect DM among Korean children and adolescents with obesity or asymptomatic glucosuria. We also recommend HbA1c level of 6.15% as the optimal cut-off point for detecting DM in Korean children and adolescents.

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1. Introduction

Diabetes mellitus (DM) is one of the most common chronic disorders in children and adolescents and is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.¹ Until recently, type 1 diabetes (T1DM) was the most frequent form of DM among young people. In the 1990s, various reports indicated that the incidence of childhood type 2 diabetes (T2DM) was increasing and this trend continues at present.^{2,3} The American Diabetes Association (ADA) and the American Academy of Pediatrics approved screening for T2DM in children because T2DM can be asymptomatic at diagnosis and requires tight glycemic control to delay the onset of chronic vascular complications.^{4,5}

Fasting plasma glucose (FPG) and 2-hour plasma glucose following an oral glucose tolerance test (2-h OGTT) have been used as the gold standard tests for diagnosis of DM.⁶ However, these tests require individuals to fast, which is an inconvenience in the clinical setting and may result in lower testing rates. Furthermore, the tests are costly and time-consuming. In contrast, hemoglobin A1c (HbA1c) is a stable indicator of chronic hyperglycemia and offers a potentially simpler, non-fasting and, therefore, more acceptable test. Furthermore, HbA1c is associated with less intra-individual variability and is more reproducible than the FPG and 2-h OGTT. The use of HbA1c for the diagnosis of DM was suggested as early as the mid-1980s.⁷ In 2010, the American Diabetes Association (ADA) included HbA1c $\geq 6.5\%$ (48 mmol/L) as a diagnostic criterion for DM, and the committee also recommended HbA1c testing for diagnostic purposes in asymptomatic adolescents.⁸ Nevertheless, the diagnostic role of HbA1c remains a controversial issue.^{9,10} HbA1c has several disadvantages in the pediatric population, and there is limited evidence on the use of HbA1c testing for the diagnosis of DM and prediabetes in children and adolescents. A recent series of pediatric studies appears to show that HbA1c has lower sensitivity than FPG or 2-h OGTT.^{11–13}

The aim of this study was to evaluate the correlation between plasma glucose (FPG and 2-h OGTT) and HbA1c and examine whether HbA1c could be used in place of the FPG and 2-h OGTT, the established ADA diagnostic criteria, in obese children or children with asymptomatic glucosuria in Korea.

2. Materials and methods

2.1. Subjects and methods

This study enrolled 190 children attending Chonbuk National University Children's Hospital for an OGTT to confirm the diagnosis of diabetes, between 2010 and 2017. Of these, 125 children had glucosuria on school urinary glucose screening, and the remaining 65 children were referred to the hospital due to obesity. Subjects were excluded if they were known to have diabetes or renal glucosuria prior to the study and if their hemoglobin levels were less than 10 g/dL. All subjects were categorized into the following groups: normal glucose tolerance (NGT), and glucose intolerance groups (which includes impaired glucose tolerance, IGT and diabetes, DM), according to the results of the OGTT.

Anthropometric measures and medical histories were collected at the first hospital visit, and height and weight measurements were converted to body mass index (BMI) percentiles, according to the 2007 Korean National Growth Charts.¹⁴ Overweight was defined as age- and sex- specific BMI ≥ 85 th and <95 th percentiles, and obesity was similarly defined as BMI ≥ 95 th percentile. Blood samples were taken in the morning after 12 h of fasting, and an OGTT (1.75 g/kg, maximum 75 g of glucose) was performed to confirm DM. DM was defined as a 2-hour plasma glucose level following OGTT (2-h OGTT) ≥ 200 mg/dL (11.1 mmol/L) or a fasting plasma glucose (FPG) ≥ 126 mg/dL (7.0 mmol/L), impaired glucose tolerance (IGT) as a 2-h OGTT 140–199 mg/dL (7.8–11.0 mmol/L), and normal glucose tolerance (NGT) as a 2-h OGTT < 140 mg/dL (7.8 mmol/L) according to the WHO criteria based on OGTT.¹⁵ FPG, total and high-density lipoprotein (HDL) cholesterol, and triglycerides were measured by enzymatic methods (Roche Diagnostics, Mannheim, Germany). HbA1c was measured via high-performance liquid chromatography (Bio-Rad Variant II, Richmond, CA, USA). Serum insulin and c-peptide were measured by immunoradiometric assay (IRIMA) using commercial kits (DIAsource ImmunoAssay S.A., Belgium for insulin; Institute of Isotopes Co., Ltd., Budapest, Hungary for c-peptide). Insulin sensitivity was estimated using the previously validated homeostasis model assessment of insulin resistance (HOMA-IR) index.¹⁶

The study was approved by the Institutional Review Board of the Clinical Research Institute of Chonbuk National University Hospital (IRB No. CUH 2018-03-048-001).

2.2. Statistical analysis

All variables are expressed as mean \pm SD. Statistical significance was defined as a p value < 0.05 for all clinical and laboratory variables. Chi-square (χ^2) and one-way analysis of variance (ANOVA) tests were performed using SPSS software (version 12.0, SPSS, Chicago, IL, USA). Pearson correlation coefficients were obtained to determine the strengths of linear associations between HbA1c levels and concentrations of FPG and 2-h OGTT. Diagnostic evaluation indicators are sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). These were calculated for each cut-off value. Optimal HbA1c and FPG cut-off values were determined using the Youden index (J), defined as "J = maximum (sensitivity + specificity - 1)". The κ statistic was calculated as a measure of agreement between ADA criteria and each indicator group, according to HbA1c, FPG, or 2-h OGTT. The use of HbA1c as a diagnostic tool for diabetes was evaluated by calculating a receiver operating characteristics (ROC) curve. The area under the ROC curve (AUC) was considered as an effective measure of the diagnostic test inherent validity.

3. Results

3.1. Clinical characteristics of the subjects with different glucose tolerance categorized by 2-h OGTT

Demographic and laboratory characteristics of the subjects are shown in Table 1. Based on the OGTT performed on 190

Table 1 Clinical characteristics of the subjects categorized by the 2-h OGTT.

Characteristic	Total	NGT	IGT	DM	P
Number (%)	190 (100.0)	117 (61.6)	33 (17.4)	40 (21.1)	
Age (years)	12.56 ± 3.44	11.79 ± 3.57	12.83 ± 3.04	14.57 ± 2.46*	0.000
Sex (%)					
Female	99 (52.1)	52 (44.4)	20 (60.6)	27 (67.5)	0.007
Male	91 (47.9)	65 (55.6)	13 (39.4)	13 (32.5)	
BMI (kg/m ²)	24.50 ± 5.12	23.95 ± 4.66	25.20 ± 6.19	25.58 ± 5.36	0.164
Obesity (%)	86 (45.3)	49 (41.9)	20 (60.6)	17 (42.5)	0.929
Family history of DM (%)	52 (39.1)	20 (30.3)	10 (37.0)	22 (55.0)	0.013
Hb (g/dL)	14.09 ± 1.17	13.85 ± 1.06*	14.04 ± 1.21*	14.97 ± 1.14 [†]	<0.001
HbA1c (%)	6.3 ± 1.8	5.5 ± 0.3*	6.1 ± 1.1 [†]	9.0 ± 2.4 [‡]	<0.001
<5.7% (NGT)	117 (61.6)	89 (83.2)	16 (14.9)	2 (1.9)	
5.7–6.4% (at risk for DM)	41 (21.6)	27 (65.9)	11 (26.8)	3 (7.3)	
≥6.5% (DM)	42 (22.1)	1 (2.4)	6 (14.3)	35 (83.3)	
FPG (mg/dL)	110.74 ± 52.92	89.20 ± 7.77*	96.24 ± 15.30*	185.70 ± 76.59 [†]	<0.001
2-h OGTT (mg/dL)	177.91 ± 127.24	115.39 ± 14.36*	158.67 ± 19.18 [†]	351.63 ± 110.16 [‡]	<0.001
Serum c-peptide (ng/mL)	2.67 ± 1.54	2.41 ± 1.37*	2.78 ± 1.21* [†]	3.33 ± 1.99 [†]	0.005
HOMA-IR	4.96 ± 5.76	3.53 ± 3.48*	4.74 ± 3.40*	10.49 ± 9.95 [†]	<0.001
Cholesterol (mg/dL)	170.07 ± 34.67	162.61 ± 33.24*	163.92 ± 26.64*	185.61 ± 36.89 [†]	0.002
HDL (mg/dL)	47.36 ± 12.09	49.57 ± 12.75	46.00 ± 11.33	44.73 ± 11.05	0.108
LDL (mg/dL)	100.26 ± 33.29	92.16 ± 31.85*	100.38 ± 27.71* [†]	112.83 ± 35.46 [†]	0.007
TG (mg/dL)	177.84 ± 67.24	101.58 ± 59.01*	115.88 ± 62.10* [†]	144.49 ± 75.14 [†]	0.005

OGTT, oral glucose tolerance test; NGT, normal glucose tolerance; IGT, impaired glucose tolerance; DM, diabetes mellitus; HbA1c, glycated hemoglobin; FPG, fasting plasma glucose; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, low-density lipoprotein; HDL, high-density lipoprotein. *, †, ‡, Identical superscript letters indicate a non-significant difference between the groups based on the Tukey multiple comparison test.

subjects, 33 (17.4%) were diagnosed with IGT, and 40 (21.1%) were diagnosed with DM. The remaining 117 students (61.6%) were diagnosed with NGT. The mean age and BMI for all subjects were 12.6 years and 24.5 kg/m², respectively. The BMI values were comparable across the 3 groups. There was an increased prevalence of female and elderly subjects among the IGT and DM groups compared to the NGT group. The mean FPG and 2-h OGTT levels in these groups were significantly higher than among subjects with NGT ($p < 0.001$). The average HbA1c level among all subjects was 6.3 ± 1.8%. As expected, HbA1c levels were significantly higher in the DM group (9.0%) than in the IGT (6.1%) or NGT group (5.5%). Furthermore, c-peptide and HOMA-IR levels in the DM group were significantly higher than in the NGT and IGT groups.

3.2. Glucose tolerance status according to HbA1c criterion

The distribution of HbA1c among the 190 subjects is shown in Table 1. Patients were categorized into 3 groups by the ADA criterion of HbA1c as follows: NGT group, 107 (55.3%) subjects; at risk for DM group, 41 (21.6%) subjects; DM group, 42 (22.1%) subjects. Although the majority (83.2%) of subjects with an HbA1c < 5.7% were classified as having NGT according to the OGTT, 16.8% of subjects were classified as having IGT or DM. Of 41 subjects in at the risk for DM group (HbA1c 5.7–6.4%), 27 (65.9%) were categorized as having NGT and 3 (7.3%) as having DM according to the OGTT. The majority (83.3%) of subjects with an

HbA1c ≥ 6.5% were classified as having DM by the OGTT, while only 1 subject (2.4%) was classified as having NGT. Therefore, of 42 subjects with DM according to HbA1c criterion, 7 (16.7%) did not meet the standard diagnostic criteria for DM. We subsequently evaluated all subjects with HbA1c ≥ 6.5% to identify any differences in clinical parameters between subjects with DM ($n = 35$) and without DM ($n = 7$) according to the OGTT. However, there are no differences in age, sex difference, HbA1c level, serum c-peptide, HOMA-IR and cholesterol profile between the 2 groups except the FPG and 2-h OGTT (no data).

3.3. The diagnostic accuracy for the detection of diabetes by FPG, 2-h OGTT and HbA1c criteria

Among 47 children categorized as having DM, 40 patients (85.1%) were diagnosed with DM by the 2-h OGTT criterion and 42 (89.4%) were diagnosed with DM according to the HbA1c criterion. The sensitivity, specificity and positive and negative predictive values for each DM diagnostic criterion are shown in Table 2. The diagnostic sensitivities of HbA1c and 2-h OGTT diagnostic criteria were significantly greater than that of the FPG (89.4%, 85.1% vs. 63.8%). This finding suggests that both the 2-h OGTT and HbA1c criteria were good predictors of DM in studied subjects. Next, we evaluated the diagnostic accuracies of HbA1c, 2-h OGTT and FPG criteria by calculating a ROC curve with the 95% confidence intervals. The AUCs for each diagnostic criterion were 0.970 for HbA1c, 0.939 for FPG, and 0.977 for 2-h

Table 2 The diagnostic accuracy of fasting plasma glucose (FPG), 2-h OGTT, and HbA1c criteria for the detection of diabetes.

		Non-DM (%)	DM (%)	Total (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P value	K coefficient	AUC
HbA1c	<6.5%	143 (100.0)	5 (10.5)	148 (77.9)	89.4	100.0	100.0	96.6	<0.001	0.927	0.970
	≥6.5%	0 (0.0)	42 (89.4)	42 (22.1)							
	Total	143 (100.0)	47 (100.0)	190 (100.0)							
FPG	<126 mg/dL	143 (100.0)	17 (36.2)	160 (84.2)	63.8	100.0	100.0	89.4	<0.001	0.727	0.939
	≥126 mg/dL	0 (0.0)	30 (63.8)	30 (15.8)							
	Total	143 (100.0)	47 (100.0)	190 (100.0)							
2-h OGTT	<200 mg/dL	143 (100.0)	7 (14.9)	150 (78.9)	85.1	100.0	100.0	95.3	<0.001	0.896	0.977
	≥200 mg/dL	0 (0.0)	40 (85.1)	40 (21.1)							
	Total	143 (100.0)	47 (100.0)	190 (100.0)							

PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve.

OGTT. These results indicate that HbA1c levels are a good screening tool in children at risk of developing DM.

3.4. Correlation between HbA1c and FPG or 2-h OGTT

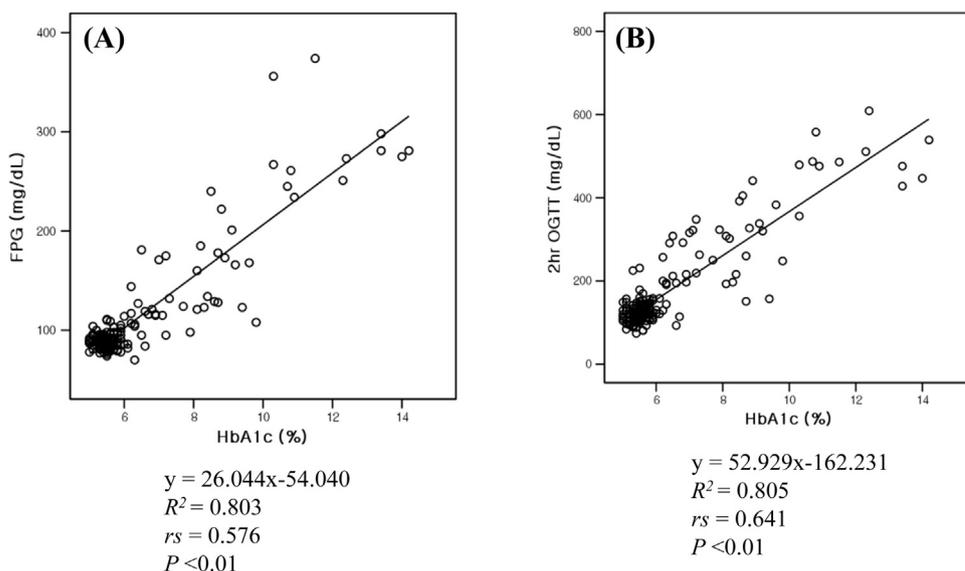
The correlations between HbA1c and FPG or 2-h OGTT were analyzed by least squares regression. As shown in Fig. 1, HbA1c levels strongly correlated with FPG and 2-h OGTT (FPG: $r_s = 0.576$, $p < 0.01$; 2-h OGTT: $r_s = 0.641$, $p < 0.01$). Mean FPG and 2-h OGTT for HbA1c values of 6.5% were calculated using regression methods as 115.2 and 181.8 mg/dL, respectively. Mean HbA1c values for FPG of 126 mg/dL and 2-h OGTT of 200 mg/dL were calculated using regression methods as 6.8% and 6.7%, respectively. We then evaluated their correlation by ROC curve analysis. Based on the ROC curves (Fig. 2A,B), the HbA1c level for DM diagnosis correlated strongly with the FPG (AUC; 0.980) and 2-h OGTT (AUC; 0.949). Furthermore, we examined

whether there were any differences in the correlation between HbA1c with 2-h OGTT according to clinical variables, such as sex and BMI, in the subjects. No significant differences in sensitivity, specificity, and AUC were observed (Fig. 2C–F). This finding suggests that the HbA1c criterion for predicting DM is a good screening tool for children, including obese girls.

The sensitivity, specificity, PPV, and NPV using different HbA1c threshold values are shown in Table 3. When the HbA1c threshold value was lowered to 6.15%, sensitivity increased to 95.7%, with a corresponding specificity of 96.5%, a PPV of 90%, and a NPV of 98.6%.

4. Discussion

This study found that HbA1c level $\geq 6.5\%$, endorsed by the ADA for the diagnosis of DM, was adequate to detect DM among Korean children and adolescents. We also proposed an HbA1c level of 6.15% as the optimal cut-off point for



Mean FPG for an HbA1c of 6.5% : 115.2 mg/dL
(6.8 % : 126 mg/dL)

Mean 2-h OGTT for an HbA1c of 6.5% : 181.8 mg/dL
(6.7 % : 200 mg/dL)

Figure 1 HbA1c correlations: correlation between FPG and HbA1c (A) and correlation between 2-h OGTT and HbA1c (B).

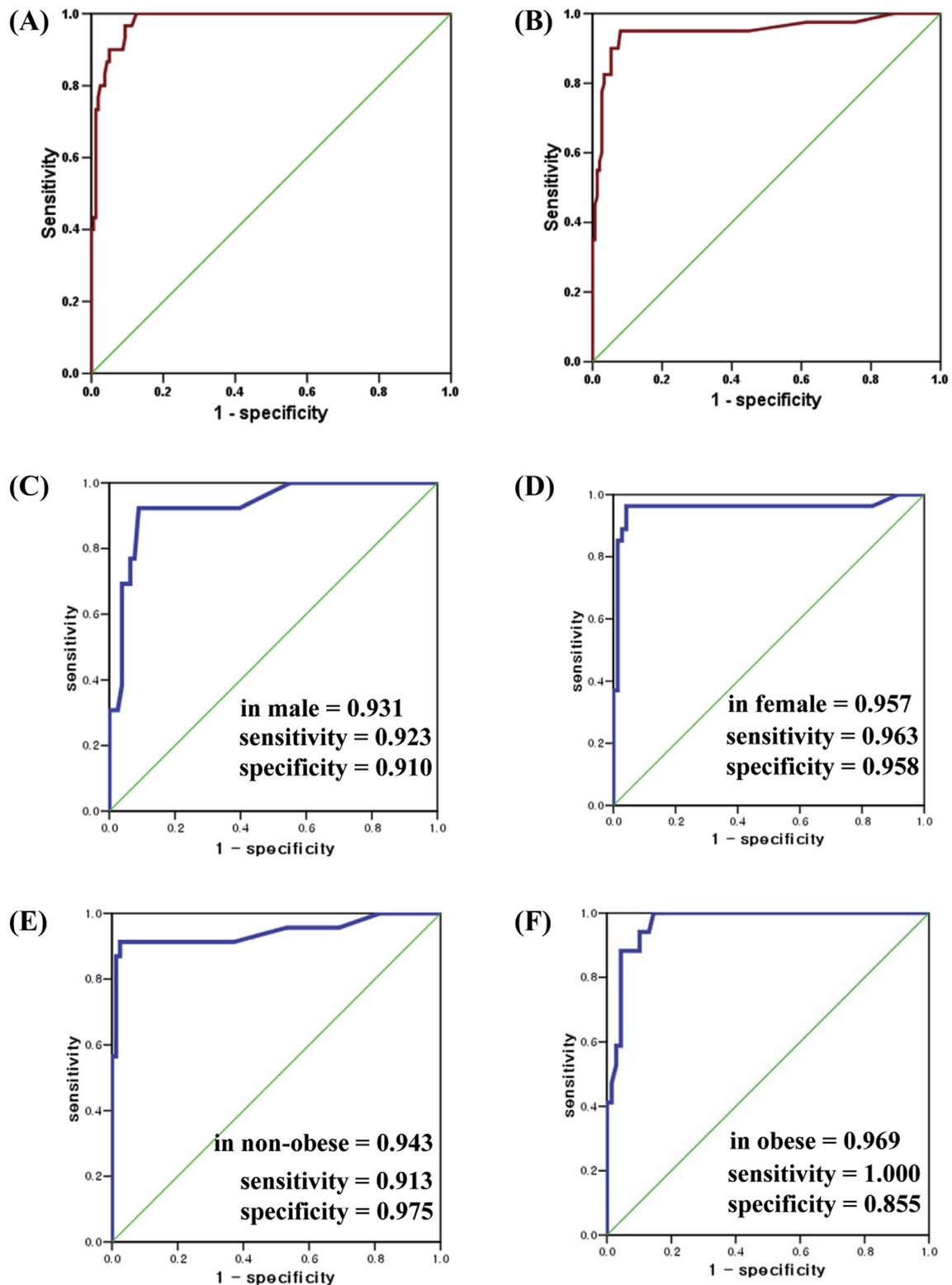


Figure 2 Receiver operating characteristic (AUC) curves comparing plasma glucose (A) and HbA1c (B) for the detection of diabetes. Correlation between HbA1c and sex (C and D)/obesity (E and F): AUC of HbA1c according to 2-h OGTT criteria.

predicting DM in children. This is the first study to evaluate the correlation between plasma glucose and HbA1c levels in Korean children at risk of diabetes.

There are increasing reports of T2DM, previously a disorder of middle-aged or elderly persons, among

children and adolescents. The likely explanation for this is the emerging youth obesity epidemic.² Several studies have shown an increased risk of microvascular complications among young adolescents with T2DM compared to those with T1DM.^{3–5} Therefore, screening for IGT and

Table 3 Sensitivities and specificities of different HbA1c levels for diagnosing DM.

HbA1c level (%)	Sensitivity	Specificity	PPV	NPV
6.05	0.957	0.951	0.865	0.986
6.15	0.957	0.965	0.900	0.986
6.25	0.915	0.972	0.915	0.972
6.35	0.915	0.993	0.977	0.973
6.45	0.894	0.993	0.977	0.966
6.50	0.894	1.000	1.000	0.966

PPV, positive predictive value; NPV, negative predictive value.

T2DM in children at risk of glucose intolerance is necessary. Although fasting plasma glucose (FPG) and 2-hour plasma glucose level following an OGTT (2-h OGTT) are the gold standard tests for the diagnosis of DM, these tests are cumbersome for both the primary care physician and the patient.⁶ In contrast, measuring HbA1c levels is more convenient for diagnosing diabetes than fasting blood glucose and OGTT. It does not require patients to fast prior to the test, has a lower intra-individual variability, and can be related to the risk of long-term diabetic complications.^{17,18} However, HbA1c testing has several potential disadvantages. HbA1c testing may fail to detect cases of T1DM, as hyperglycemia develops over a short period of time. HbA1c may also vary with age and different ethnic groups.¹⁹ Furthermore, many factors related to red blood cell lifespan, such as iron deficiency anemia, sickle cell disease, and thalassemia, could affect HbA1c levels.²⁰

The diagnosis of diabetes in pediatric populations, including HbA1c testing, is the same as for adults.⁸ The cut-off value of FPG and OGTT for diagnosing diabetes is based on long-term follow up of chronic diabetic retinopathy or nephropathy. Therefore, the question may be whether it is appropriate for this paper to use fasting glucose and OGTT as the gold standard to determine the cut-off value of HbA1c. Previous studies^{21,22} have found strong correlations between HbA1c and plasma glucose in adult populations. However, HbA1c testing has several potential disadvantages in the pediatric population, and data have largely been extrapolated from adult populations.¹³ Recent pediatric studies have dismissed the use of HbA1c levels $\geq 6.5\%$ for the diagnosis of diabetes because of the lack of correlation with the OGTT.^{11–13} Ogawa et al.²³ reported that HbA1c strongly correlated with plasma glucose in children with DM detected by a urine glucose screening program. However, the mean glucose values of the 2-h OGTT and the FPG corresponding to HbA1c levels of 6.5% in Japanese children were found to be lower than those in Japanese adults. Furthermore, Hosking et al.²⁴ reported that the positive association between HbA1c and FPG throughout childhood was weak and their trends diverge from 10 years, limiting the interpretation of HbA1c for the diagnosis of impaired fasting glucose (IFG) during childhood. In the present study, HbA1c levels were found to be strongly correlated with FPG and 2-h OGTT. The mean values derived from FPG and 2-h OGTT corresponding to an HbA1c of 6.5% were 115.2 and 181.8 mg/dL, respectively. Mean HbA1c level for FPG of

126 mg/dL was 6.8% and for 2-h OGTT of 200 mg/dL was 6.7%. These values are lower than 7.5% and 7.8% in Japanese children.²³ We also evaluated the correlation between HbA1c and 2-h OGTT according to sex and BMI. However, there was no significant difference in sensitivity, specificity, and AUC, according to sex and BMI. This suggests that the HbA1c criterion for predicting DM subjects is a good screening tool for children, including obese girls. This finding is consistent with a study by Shah et al. reporting that HbA1c was a good predictor of type 2 DM in obese young people.²⁵ However, other studies^{12,26} found that HbA1c had poor discriminatory capacity and this could lead to a failure to detect dysglycemia in obese children. This discrepancy may be due to the small number of subjects, ethnic variation, and age difference of the study populations.

According to the annual school urine screening program in Korea, glycosuria is detected in over 3000 students per year and they are advised to be evaluated for diabetes.²⁷ Although many children with asymptomatic glucosuria have been diagnosed with T2DM by OGTT, the recapture rate for OGTT was low in Korean schoolchildren.²⁷ If the more convenient HbA1c criterion were applied in the clinical setting, the low recapture rate might be improved and more DM subjects would be detected. According to a recent study, 58% of US physicians who provide primary care to adolescents ordered HbA1c as part of their battery of initial tests for screening adolescents with T2DM.²⁸ It is important to be aware of the correlation between FPG and HbA1c when using HbA1c as a diagnostic criterion for DM in children. In the current study, 83.3% of subjects with HbA1c $\geq 6.5\%$ were diagnosed with DM by the OGTT. Conversely, 12.5% of subjects with DM diagnosed by the OGTT had HbA1c levels $<6.5\%$. Because PG levels and HbA1c levels reflect different aspects of glucose metabolism, there is always a risk of failing to identify patients who would have been diagnosed by an OGTT. Therefore, in the present study, we proposed a HbA1c level of 6.15% as the optimal cut-off point for predicting DM in children. Lee H et al.²⁹ recently reported that an HbA1c threshold of 6.1% was the optimal limit for diagnosing diabetes, with 63.8% sensitivity and 88.1% specificity in Korean adults.

There were some limitations to this study. The number of cases was relatively small; therefore, analysis according to IGT and DM subgroups was challenging. In addition, this study included selected students with glucosuria on school urine screening program and obese students. A study including a large number of children and adolescents with normal clinical parameters is, therefore, necessary.

In conclusion, this study found that HbA1c criterion $\geq 6.5\%$, endorsed by the ADA/WHO as diagnostic criteria for DM, was adequate to detect DM among Korean children and adolescents with obesity or asymptomatic glucosuria. Although there was good agreement between the HbA1c and 2-h OGTT criterion for the diagnosis of DM, we suggest HbA1c level of 6.15% as the optimal cut-off point for detecting DM in Korean children and adolescents. Finally, the high diagnostic efficacy of HbA1c may contribute to the early detection of asymptomatic children and adolescents with DM.

Conflict of interest

The authors declare that they have no conflict of interest.

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References

- Daneman D. Type 1 diabetes. *Lancet* 2006;**367**:847–58.
- Gungor N, Hannon T, Libman I, Bacha F, Arslanian S. Type 2 diabetes mellitus in youth: the complete picture to date. *Pediatr Clin North Am* 2005;**52**:1579–609.
- Harron KL, Feltbower RG, McKinney PA, Bodansky HJ, Campbell FM, Parslow RC. Rising rates of all types of diabetes in south Asian and non-south Asian children and young people aged 0-29 years in West Yorkshire, UK, 1991–2006. *Diabetes Care* 2011;**34**:652–4.
- Type 2 diabetes in children and adolescents. American Diabetes Association. *Pediatrics* 2000;**105**:671–80.
- Krebs NF, Himes JH, Jacobson D, Nicklas TA, Guilday P, Styne D. Assessment of child and adolescent overweight and obesity. *Pediatrics* 2007;**120**:S193–228.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2007;**30**:S42–7.
- Simon D, Coignet MC, Thibault N, Senan C, Eschwège E. Comparison of glycosylated hemoglobin and fasting plasma glucose with two-hour post load plasma glucose in the detection of diabetes mellitus. *Am J Epidemiol* 1985;**122**:589–93.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;**33**:S62–9.
- Malkani S, DeSilva T. Controversies on how diabetes is diagnosed. *Curr Opin Endocrinol Diabetes Obes* 2012;**19**:97–103.
- Sacks DB. A1C versus glucose testing: a comparison. *Diabetes Care* 2011;**34**:518–23.
- Kapadia CR. Are the ADA hemoglobin A(1c) criteria relevant for the diagnosis of type 2 diabetes in youth? *Curr Diab Res* 2013;**13**:51–5.
- Lee JM, Gebremariam A, Wu EL, LaRose J, Gurney JG. Evaluation of nonfasting tests to screen for childhood and adolescent dysglycemia. *Diabetes Care* 2011;**34**:2597–602.
- Lee JM, Wu EL, Tarini B, Herman WH, Yoon E. Diagnosis of diabetes using hemoglobin A1c: should recommendations in adults be extrapolated to adolescents? *J Pediatr* 2011;**158**:947–52.
- Moon JS, Lee SY, Nam CM, Choi JM, Choe BK, Seo JW, et al. 2007 Korean national growth charts: review of developmental process and an outlook. *Korean J Pediatr* 2008;**51**:1–25.
- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998;**15**:539–53.
- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;**28**:412–9.
- Selvin E, Crainiceanu CM, Brancati FL, Coresh J. Short-term variability in measures of glycemia and implications for the classification of diabetes. *Arch Intern Med* 2007;**167**:1545–51.
- Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 1997;**20**:1183–97.
- Kamps JL, Hempe JM, Chalew SA. Racial disparity in A1C independent of mean blood glucose in children with type 1 diabetes. *Diabetes Care* 2010;**33**:1025–7.
- Tarim O, Küçükerdoğan A, Günay U, Eralp O, Ercan I. Effects of iron deficiency anemia on hemoglobin A1c in type 1 diabetes mellitus. *Pediatr Int* 1999;**41**:357–62.
- Ito C, Maeda R, Ishida S, Sasaki H, Harada H. Correlation among fasting plasma glucose, two-hour plasma glucose levels in OGTT and HbA1c. *Diabetes Res Clin Pract* 2000;**50**:225–30.
- Bonora E, Calcaterra F, Lombardi S, Bonfante N, Formentini G, Bonadonna RC, et al. Plasma glucose levels throughout the day and HbA(1c) interrelationships in type 2 diabetes: implications for treatment and monitoring of metabolic control. *Diabetes Care* 2001;**24**:2023–9.
- Ogawa E, Urakami T, Suzuki J, Yoshida A, Takahashi S, Mugishima H. Usefulness of HbA1c to diagnose diabetes among Japanese children detected by a urine glucose screening program in the Tokyo metropolitan area. *Endocr J* 2012;**59**:465–71.
- Hosking J, Metcalf BS, Jeffery AN, Streeter AJ, Voss LD, Wilkin TJ. Divergence between HbA1c and fasting glucose through childhood: implications for diagnosis of impaired fasting glucose (Early Bird 52). *Pediatr Diabetes* 2014;**15**:214–9.
- Shah S, Kublaoui BM, Oden JD, White PC. Screening for type 2 diabetes in obese youth. *Pediatrics* 2009;**124**:573–9.
- Nowicka P, Santoro N, Liu H, Lartaud D, Shaw MM, Goldberg R, et al. Utility of hemoglobin A(1c) for diagnosing prediabetes and diabetes in obese children and adolescents. *Diabetes Care* 2011;**34**:1306–11.
- Korean School Health Association (KSHA). Available at <http://www.ksha.or.kr>. Accessed July 19, 2015.
- Lee JM, Eason A, Nelson C, Kazzi NG, Cowan AE, Tarini BA. Screening practices for identifying type 2 diabetes in adolescents. *J Adolesc Health* 2014;**54**:139–43.
- Lee H, Oh JY, Sung YA, Kim DJ, Kim SH, Kim SG, et al. Optimal hemoglobin A1C cutoff value for diagnosing type 2 diabetes mellitus in Korean adults. *Diabetes Res Clin Pract* 2013;**99**:231–6.