Value of 1-Hour Plasma Glucose During an Oral Glucose Tolerance Test in a Multiethnic Cohort of Obese Children and Adolescents

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ABSTRACT

One hour plasma glucose (1-hr PG) concentration during an oral glucose tolerance test (OGTT) is steadily emerging as an independent predictor of type 2 diabetes (T2D).

METHODS: We applied the current cut off thresholds reported in the pediatric literature for the 1-hr PG, 132.5 (7.4 mmol/l) and 155 mg/dL (8.6 mmol/l) during an OGTT, to report abnormal glucose tolerance (AGT) using ROC curve analyses. We determined the empirical optimal cut point for 1-hr PG for our multi ethnic cohort using the Youden Index.

RESULTS: About 1-hour and 2-hours plasma glucose showed the highest predictive potential based on Areas under the curve (AUC) values of 0.91 [CI: 0.85, 0.97] and 1 [CI: 1, 1], respectively. Further comparison of the ROC curves of the 1-hour and 2-hour PG measurements as predictors of an abnormal OGTT showed that their associated AUCs differed significantly ($X^2(1) = 9.25$, $P < .05$). Using 132.5 mg/dL as the cutoff point for plasma glucose at 1-hour yielded a ROC curve with an AUC of 0.796, a sensitivity of 88%, and a specificity of 71.2%. Alternatively, the cutoff point of 155 mg/dL resulted in a ROC AUC of 0.852, a sensitivity of 80%, and a specificity of 90.4%.

CONCLUSION: Our cross-sectional study affirms that the 1-hr PG can identify obese children and adolescents at increased risk for prediabetes and/or T2D with almost the same accuracy as a 2-hr PG. In our multi-ethnic cohort, a 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) serves as an optimal cut-point, using the estimation of the Youden index with AUC of 0.86 and sensitivity of 80%.We support the petition to consider the 1-hr PG as integral during an OGTT, as this adds value to the interpretation of the OGTT beyond the fasting and 2-hr PG.

KEYWORDS: 1-Hour plasma glucose, oral glucose tolerance test, obese adolescents, insulin resistance, diabetes

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Introduction

The worldwide rate of type 2 diabetes (T2D) is increasing at epidemic proportions. According to the International Diabetes Foundation there are 537 million adults (20-79 years) living with T2D and this number is expected to rise to 643 million by 2030. It is noteworthy that 1 out of 2 adults (240 million) have diabetes but are undiagnosed.[1] The increase in T2D prevalence has aligned with increased cardiovascular morbidity and mortality in people with diabetes, despite the decrease in adverse cardiovascular outcomes in individuals without diabetes in the same time period.[2]

Though commonly considered an adult disease, T2D has steadily become a relevant health condition in youths.[3] Therefore, identifying reliable markers to identify individuals at high-risk for future diabetes is important to facilitate early intervention. Prediabetes was introduced in 1997 by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus including 2 categories namely, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT)[4]. In spite of this, epidemiological studies have demonstrated that there are, in fact, limitations of strictly relying on IFG and IGT for predicting risk as only one-half of those with IGT convert to T2D within 10 years of follow-up. In addition, nearly 40% of individuals who develop T2D exhibit normal glucose tolerance (NGT) at baseline.[5]

The traditional glycemic markers fasting plasma glucose (FPG), 2 hours plasma glucose (2-hr PG), and HbA1c are used in predicting future risk of diabetes. While the oral glucose tolerance test (OGTT) is an important standard method for identifying individuals at risk for developing T2D,[6] it has

poor reproducibility in children and adolescents.[7] Weiss et al[7] showed that 45% of children with IGT at baseline reverted back to NGT, while 24% of those with IGT progressed to diabetes in a 2year follow up.

Recent studies have demonstrated that the 1 hour plasma glucose (1-hr PG) concentration during an OGTT is steadily emerging as an independent predictor of T2D in adults.[8,9] Abdul-Ghani et al[10,11] demonstrated that a 1-hr PG concentration ⩾155 mg/dL (8.6 mmol/l) served as a marker for the development of T2D in two independent cohorts. These studies, among others, demonstrated that the 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) was a far better predictor of T2D than both FPG and 2-hr PG concentrations, with the 1-hr PG test yielding maximal sum of sensitivity 75% and specificity 79%.[10,11] The 1-hr PG has also been shown to predict risk for T2D with greater sensitivity than HbA1c.[12]

Furthermore, the 1-hour plasma glucose has generally been found to be a more sensitive predictor of progression to T2D, complications and mortality than the 2-hr PG.[13,14] The 1-hr PG is also associated with increased risk for non-alcoholic fatty liver disease and hepatic fibrosis.[15]

Children and adolescents from high-risk ethnic groups are at particular risk for accelerated progression to T2D despite implementation of lifestyle changes.[16] Therefore, the 1-hr PG may provide a valuable opportunity to identify high-risk obese adolescents especially those who are insulin resistant who may need to be monitored closely with serial OGTTs to assess their evolving risk for T2D. Abdul-Ghani et al[17] showed in 1551 non-diabetic adults followed for 7 to 8 years that a high 1-hr PG in those with NGT was just as effective as other models for predicting diabetes. Since then, several longitudinal studies in different populations (follow-up ranging from 4 to 39 years) have validated that the 1-hr PG is highly predictive for detecting progression to T2D.[18-21] Furthermore, the STOP DIABETES trial demonstrated the efficacy of lifestyle intervention and pharmacotherapy in a subset of individuals with NGT and 1-hr PG > 155 mg/dL (8.6 mmol/l) in halting progression to T2D.[22] An elevated 1-hr PG > 155 mg/dL (8.6 mmol/l) has been reported in as many as 12% of obese youth with NGT and 57% of those with IGT and therefore may be the earliest marker of dysglycemia.[23]

Although other cutoff values may also identify high-risk individuals, the 155 mg/dL (8.6 mmol/l) level in adults appears to be practical to otherwise avoid capturing too large a segment of the population.[24] The 1-hr PG cut off has also been studied in youth. Manco et al[24] and Tfayli et al[25] identified a lower 1-hr PG cutoff value of 132.5 mg/dL (7.4 mmol/l) in 2 independent cohorts of obese youths demonstrating enhanced sensitivity and specificity versus the 155 mg/dL (8.6 mmol/l) threshold.

While several pediatric studies have highlighted the relevance of the 1-hr PG on the spectrum of glucose dysregulation,[24-26] there is a lack of consensus regarding the appropriate cut point. We proposed to apply the current suggested cutoff thresholds in youth for the 1-hr PG, 132.5 (7.4 mmol/l) and 155 mg/dL (8.6 mmol/l) to our multi-ethnic cohort of Hispanic, African-American (AA) and Asian children and adolescents.

Our objectives were to use (1) receiver operating characteristic (ROC) curves to explore the predictive potential of continuous metabolic measures: HbA1c, fasting plasma glucose (FPG), 1-hour plasma glucose, and 2-hours plasma glucose obtained during an OGTT on binary OGTT outcome (normal vs abnormal); (2) to analyze the 1-hr PG that could serve as an optimal cut point for predicting abnormal glucose tolerance (AGT) in our multi ethnic cohort.

Methods

This study was a retrospective chart review (Institutional Review Board [IRB] approved) of records of children and adolescents seen at New York University Grossman School of Medicine and Health and Hospitals Corporation Health Systems from 2015 to 2021. The study was reviewed by the Institutional Review Board of New York School of Medicine as an expedited chart review and was approved (IRB# 17-00361). As the design was a retrospective chart review using de-identified data, parents were not consented.

The children and adolescents were overweight or obese and often had related co-morbidities including polycystic ovary syndrome, dyslipidemia, hypertension, acanthosis nigricans, and metabolic syndrome. On an average, we perform about 10 OGTTs in our clinic per week as standard of care for understanding the glucose and insulin dynamics in children and adolescents with prediabetes. The OGTT was performed after an overnight fast with a glucose solution (Glucola) consumed under supervision, at a dose of 1.75 g/kg of glucose to a maximum of 75 g. Samples for plasma glucose collected at 0, 60, and 120 minutes and a fasting insulin level were obtained. Based on ADA criteria,[27] NGT was defined as a fasting plasma glucose (FPG) ⩽100 mg/dL (5.6 mmol/l) and 2-hour PG ⩽ 140 mg/dL (7.8 mmol/l); IFG was defined as a FPG between 100 and 125 mg/dL (5.6 and 6.9 mmol/l); IGT was defined as a 2-hour PG level between 140 and 199 mg/dL (7.7 and 11.1 mmol/l). Patients who met the definition for IFG and/or IGT were considered to have prediabetes. Those with FPG ⩾ 126 mg/dL (7.0 mmol/l) and/or 2-hour PG ⩾ 200 mg/dL (11.1 mmol/l) were diagnosed with T2D. Glucose analysis was performed by the glucose hexokinase II method (Siemens, Tarrytown, NY), and insulin analysis was performed by radioimmunoassay (Quest Diagnostics, Teterboro, NJ). We also measured a comprehensive metabolic panel and lipid profile. Physical exam and Tanner staging was recorded on all children and adolescents as part of their clinical evaluation during the visit.

Participants who had IFG in the absence of IGT (n = 9) were excluded from the sample as the definition of abnormal glucose tolerance included only those with IGT.[27] Furthermore, individuals with incomplete data for fasting, 1-hour, and

2-hour plasma glucose measurements (n = 6) were also dropped from the sample. The final sample for analysis consisted of 129 participants.

We included children and adolescents who underwent an OGTT, irrespective of their weight percentile on the CDC charts (https://www.cdc.gov/growthcharts/index.htm) as we wanted to assess predictive value of the 1-hr PG. Though the risk for developing T2D is fourfold higher in obese versus normal weight children, more recently, Cioana et al[28] reported that only 75.3% of the 8900 children analyzed were obese at the time of diagnosis of T2D, which negates the common dictum that obesity is a universal phenotype of children and adolescents with T2D. We wanted to analyze a real world representation of children and adolescents who had an OGTT in our clinic. We ruled out T1D in all normal weight children by measuring C-peptide, insulin levels, and pancreatic autoantibodies.

Statistical analysis

Statistical analyses were performed using Stata Version 17. For analytic purposes, those with IGT or T2D were reclassified as abnormal glucose tolerance (AGT). Univariate analyses were conducted on all variables of interest in order to describe the sample. Continuous data were summarized using mean and standard deviation or median and interquartile range, depending on distribution. Categorical data were summarized by frequency and percentage.

Receiver operating characteristic (ROC) curves were utilized in order to explore the predictive potential of several continuous metabolic measures: HbA1c, FPG), 1-hour plasma glucose, and 2-hour plasma glucose during the OGTT on binary OGTT outcome (normal vs abnormal). Areas under the curve (AUC) were compared using the roc comp command in Stata, which compares AUCs based on the methods outlined by DeLong et al.[29]

ROC curve analyses were also utilized to compare the potential of several different cut points for the 1- and 2-hour plasma glucose values. For the purpose of this paper, the empirical optimal cut point for 1-hour plasma glucose value was calculated using the Youden Index, *J*. This index is equal to sensitivity + specificity – 1.[30] The higher the statistic, the closer the diagnostic test is to being "perfect" in its classification of cases. In other words, this method is helpful in identifying the threshold where *J* is maximized, indicating the most equal balance between sensitivity and specificity. Each cut point was described using AUC, 95% confidence interval of AUC, sensitivity, specificity, number of cases correctly classified, positive predictive value (PPV), and negative predictive value (NPV).

Finally, a binary logistic regression model was utilized to investigate whether the potential of an empirical optimal cut point of 1-hour plasma glucose to classify OGTT result (normal vs abnormal) remained after controlling for several clinically relevant covariates. Stepwise regression was avoided in order to maximize generalizability of the results. All assumptions for logistic regression were adequately met.

Indices of sensitivity. Homeostatic model of insulin resistance (HOMA-IR) is a validated measure of insulin sensitivity calculated as follows = [Fasting plasma insulin (FPI, in μIU/mL) × Fasting plasma glucose (FPG, in mmol/L)]/22.5.[25] Higher HOMA-IR predicts the development of T2DM in high- risk populations.[31]

Quantitative insulin-sensitivity check index (QUICKI) = 1/[log (I0) + log (G_0)] where I0 and G_0 are the fasting insulin in μIU/mL and fasting glucose in mg/dL. It has been validated against insulin sensitivity Si derived from an insulin clamp study.[32]

Indices of insulin secretion. We used Homeostatic model of beta cell function (HOMA-β), an index of secretion as HOMA-β = [20 × fasting insulin (μIU/ml)/fasting glucose (mmol/l) – 3.5].[33]

Results

One hundred fifty-two children and adolescents underwent an OGTT. Of these, 19 were pre-pubertal (Tanner 1) and 27 had HbA1c between 5.1% and 5.6% and therefore did not meet the ADA criteria for prediabetes but nonetheless underwent an OGTT related to risk factors including an elevated BMI, strong family history of diabetes, and/or symptoms of polyuria or polydipsia. The subjects did not have to meet the ADA HbA1c criteria of prediabetes (HbA1c 5.7%-6.4%) but were included in the analysis.

Results by ethnicity

Table 1 (n = 129) shows demographic and metabolic parameters of the multiethnic cohort which included Hispanic (82); African-American[30]; Asians,[17] with more female (63.7%; n = 82) than male subjects (n = 47). There were no Caucasians reflecting the clinical population from which patients were sampled. Based on weight % (CDC growth charts: 5%-85% normal weight, 85%-95% overweight; >95% obese) 28 (21%) were normal weight; 33 (25%) were overweight and 68 (54%) obese. Of those who underwent an OGTT, 104 (80.7%) had NGT, 19 (14.7%) subjects had IGT and 2 subjects (1.5%) combined IFG + IGT. Four subjects (3.1%) were diagnosed with T2D (2 Hispanic, 1 AA, and 1 Asian). Among those with NGT, 1-hr PG was <155 mg/dL in 94 mg/dL (72.9%) and ⩾155 mg/dL in 10 (7.8%). Among the ethnic group Asians adolescents were younger (mean ± SD) 12 ± 3.5 years and had lower weight 64 ± 23 kg when compared to Hispanic and AA peers (age: 14 ± 2.9 and 13.2 ± 3.6 years) and (weight: 90 ± 29 and 86 ± 34 kg; *P* = .001 and .005, respectively).

Obese adolescents were more likely to be insulin resistant (HOMA-IR cut off value of 3.4, Brar et al,[34] with 51 being insulin sensitive (IS: HOMA-IR ⩽ 3.4) and 78 insulin resistant (IR: HOMA-IR ⩾ 3.4). All those with IR had HbA1c ⩾ 5.7%. The IS group were younger (13.55 years vs 14.2 years), leaner (74.5 kg vs 90 kg) and had lower 1-hr PG when compared to the IR (121 ± 28 mg/dL vs 142 ± 4 mg/dL).

Table 1. Demographic and metabolic data the cohort (n = 129).

Demographics	
Age (years)	13.9 (3.3)
Gender	
Male	47 (36.4%)
Female	82 (63.6%)
Race	
Hispanic	82 (63.6%)
African American	30 (23.2%)
Asian	17 (13.2%)
Weight (kg)	83 (30.6)
Height (cm)	159.9 [150.7, 165.7]
BMI	32.2 (8.2)
Metabolic parameters	
HbA1c	5.9 [5.7, 6.1]
ALT	24 [17, 36]
AST	24 [21, 34]
TC	151 [134, 174]
Triglycerides	99 [71, 144]
HDL	41 [35, 50]
LDL	90 [78, 104.6]
FPG	85 [80, 91]
1-hr PG	127 [110, 152]
2-hr PG	116 [101, 134]
FPI	23.6 [13.3, 45.8]
Indices of insulin resistance	
HOMA-IR	4.5 [2.2, 8.2]
QUICKI	0.3 [0.28, 0.33]

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase (units for both in U/L); FPG, fasting plasma glucose; FPI, fasting plasma insulin (mIU/L); HDL, high density lipoprotein; HOMA-IR:-homeostatic model of insulin resistance; LDL- high density lipoproteins (all values in mg/dL); 1-hr PG, 1-hour plasma glucose; 2-hr PG, 2 hours plasma glucose during the 75 g OGTT (all values in mg/dL, to convert to mmol/l divide by 18); QUICKI, quantitative; TC, total cholesterol.
Nonparametric: median [25%, 75%]; parametric: mean (standard deviation); categorical: frequency (%).
Values shown as mean ± standard deviation.

Fasting and 2-hr PG had a positive correlation with total cholesterol ($r = .3$; $P = .009$) and triglycerides ($r = .2$; $P = .034$ and .01), respectively while 1-hr PG had a positive correlation with total cholesterol ($r = .2$; $P = .034$). No correlation was seen between PG levels and liver enzymes.

ROC curves

Figure 1 shows the performance of parameters (FPG, 1-hr PG, 2-hr PG, and HbA1c). Of the 4 measurements, 1-hour and 2-hour plasma glucose showed the highest predictive potential based on AUC values of 0.91 [CI: 0.85, 0.97] and 1 [CI: 1, 1], respectively. Further comparison of the ROC curves of the 1-hr and 2-hr PG measurements as predictors of an abnormal OGTT showed that their associated AUCs differed significantly ($X^2(1) = 9.25$, $P < .05$).[29]

1-hr PG threshold testing

The key analysis was to identify the optimal cutoff value for plasma glucose at the 1-hour time point during the OGTT (Table 2). First, ROC curve analyses were conducted to compare the 2 cut points deemed as "optimal" at the 1-hour time point in previous publications. Using 132.5 mg/dL (7.36 mmol/l) as the cutoff point for plasma glucose at 1-hour yielded a ROC curve with an AUC of 0.796, a sensitivity of 88%, and a specificity of 71.2%. Alternatively, the cutoff point of 155 mg/dL (8.6 mmol/l) resulted in a ROC AUC of 0.852, a sensitivity of 80%, and a specificity of 90.4%. Empirical optimal cut point estimation using the Youden Index identified 155.5 mg/dL (8.6 mmol/l) as the best cut point for these data, with an AUC of 0.857, sensitivity of 80%, and specificity of 91.4%. The AUCs for the 155 (8.6 mmol/l) and the 132.5 mg/dL (7.35 mmol/l) cut points were not significantly different ($X^2(1) = 1$, $P = .3173$). In contrast, as shown in Table 3, 2-hour plasma glucose demonstrated relatively low specificity and positive predictive value within the lower 50% of the plasma glucose readings at this time point for the sample.

Table 4 shows the association between 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) during the OGTT. A binary logistic regression analysis was conducted to investigate whether the 155.5 mg/dL (8.6 mmol/l) cut off point was still a reliable predictor of abnormal OGTT result after accounting for age, race/ethnicity, HbA1c, and weight (Table 4). The final logistic regression model was significant ($X^2(6, N = 129) = 58.9$, $P < .001$). With all other variables held constant, individuals who had a plasma glucose value ⩾155.5 mg/dL (8.6 mmol/l) at 1 hour were 55 times [CI: 12.9-237] more likely to have an abnormal OGTT result compared to their counterparts with a plasma glucose measurement <155.5 mg/dL (8.6 mmol/l) at 1 hour.

Discussion

The 1-hr PG provides crucial information about risk for progression to T2D as has been shown in several longitudinal adult studies[19,21,23], one pediatric study.[35] Our cross sectional study affirms that the 1-hr PG can identify obese children and adolescents at increased risk for prediabetes and/or T2D with

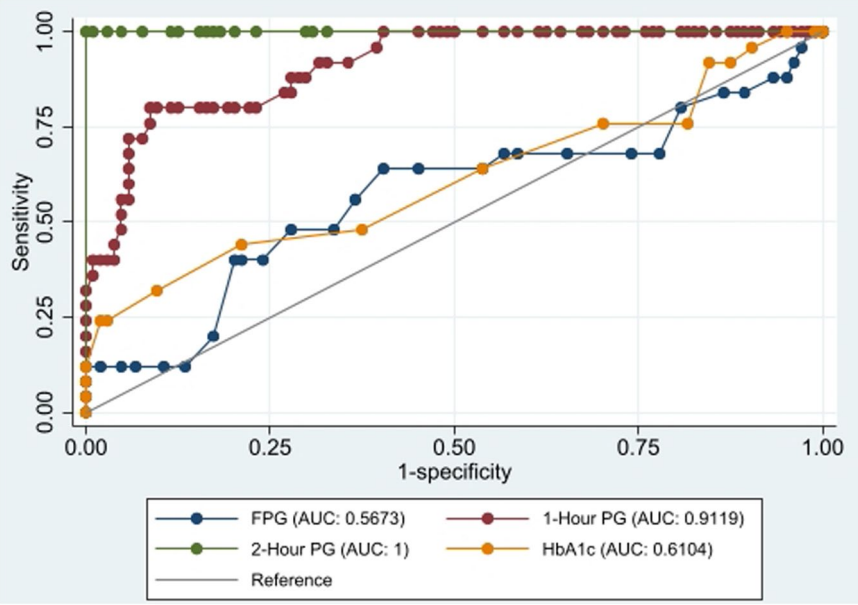

Figure 1. Performance of various continuous metabolic measures in the classification of OGTT result (normal vs abnormal) (n = 129).

Table 2. Potential for 1-hour plasma glucose as a classifier for abnormal OGTT result at previously suggested cut points and empirical optimal cut point (n = 129).

CUTOFF POINT (INCLUSIVE)	ROC AUC	[95% CI]	SENSITIVITY (%)	SPECIFICITY (%)	CORRECTLY CLASSIFIED (%)	PPV (%)	NPV (%)
1-hr PG ⩾ 132.5 mg/dL	0.796	[0.72, 0.87]	88.00	71.15	74.40	42.30	96.10
1-hr PG ⩾ 155 mg/dL	0.852	[0.76, 0.93]	80.00	90.38	88.37	66.70	94.90
1-hr PG ⩾ 155.5 mg/dL (Empirical optimal cut point)	0.857	[0.77, 0.94]	80.00	91.35	89.15	69.00	95

almost the same accuracy as a 2-hr PG. In our multiethnic cohort, a 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) serves as an optimal cut point using the estimation of the Youden index with AUC of 0.86 and sensitivity of 80%. We propose that clinicians consider obtaining a 1-hr PG during an OGTT especially in high-risk children and adolescents (eg, strong family history of T2D, rapid weight gain, and symptoms of polyuria and polydipsia).

In 1979, the National Diabetes Data Group recommended using interim glucose values including 30, 60, and 90 minutes time points during an OGTT to define IGT, though later suggested using only a fasting and post load 2-hr PG for this purpose due to convenience; these standards were later adopted by ADA and WHO.[36] The San Antonio Heart Study conducted in 1611 Mexican Americans in 2008 raised the importance of the 1-hr PG as this performed even better than the 2-hr PG in predicting progression to diabetes in the subsequent 7 to 8 years (AUC was 0.84 vs 0.79 for 1 and 2-hr PG, respectively). The hazard ratio for those developing diabetes increased significantly from 3.4 to 15.2 in those with a 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) and metabolic syndrome compared to those with an isolated elevation in the 1-hr PG.[11] Since the San Antonio Heart Study, several adult studies have confirmed the value of 1-hr PG as a discriminative predictor of progression which was validated in long-term outcome studies ranging from 12 to 39 years.[19,21,23] Furthermore, an elevated 1-hr PG in those with IGT was associated with a greater risk for developing T2D than in those with isolated IGT.[19,20] Cohort studies in the Asian population established different cut offs for the 1-hr PG with 144 mg/dL (8.0 mmol/l) identified in the Korean adult population[37] and 205 mg/dL (11.4 mmol/l) as a predictor of T2D in Japanese adults.[38] Despite these differences, the 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) represents a reasonable compromise in terms of sensitivity and specificity in most populations studied.

The traditional glycemic markers (FPG and 2-hr PG, HbA1c) have limitations in children and adolescents for predicting future risk of diabetes. Manco et al[23] in a cross-sectional study of adolescents with NGT (n = 113) found that those with 1-h PG ⩾ 155 mg/dL (8.6 mmol/l) were more likely to exhibit IGT. In addition, those with 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l), independent of glucose tolerance status, were found to exhibit

Table 3. Potential for 2-hour plasma glucose as a classifier for abnormal OGTT result at median, lower, and upper bounds (n = 129).

CUTOFF POINT (INCLUSIVE)	ROC AUC	[95% CI]	SENSITIVITY (%)	SPECIFICITY (%)	CORRECTLY CLASSIFIED (%)	PPV (%)	NPV (%)
2-hr PG ⩾ 101 mg/dL	0.654	[0.61, 0.7]	100	30.77	44.19	25.8	100
2-hr PG ⩾ 116 mg/dL	0.798	[0.75, 0.85]	100	59.82	67.44	37.3	100
2-hr PG ⩾ 134 mg/dL	0.962	[0.94, 0.99]	100	92.31	80.62	75.8	100

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; ROC AUC, receiver operator curve, area under the curve.

Table 4. Association between plasma glucose greater than or equal to 155.5 mg/dL at 1 hour during OGTT and abnormal OGTT result.

LOGISTIC REGRESSION						
ABNORMAL OGTT	COEFFICIENT ODDS RATIO (OR)	STANDARD ERROR	*T*-VALUE	*P*-VALUE	[95% CI]	SIG
PG ⩾ 155.5 mg/dL at 1 h	55.262	41.054	5.40	0	[12.885, 237.017]	*
Age (y)	1.101	0.145	0.73	.463	[0.851, 1.426]	
Race/Ethnicity						
Hispanic (ref.)	.	.	.	.	.	
African American	7.102	5.95	2.34	.019	[1.375, 36.688]	*
Asian	3.92	4.027	1.33	.184	[0.523, 29.357]	
HbA1c	1.432	0.766	0.67	.502	[0.502, 4.084]	
Weight (kg)	1.001	0.014	0.09	.93	[0.975, 1.028]	
Constant	0.001	0.002	–2.10	.036	[0, 0.61]	*
Pseudo *r*-squared	0.464	Number of observations	129			
Chi-square	58.875	Probability > chi^2	0.000			

*$P < .05$.

lower insulin secretion (ie, disposition index measured using the hyperinsulinemic euglycemic clamp) relative to insulin sensitivity compared to those with 1-hr PG < 155 mg/dL (8.6 mmol/l).[25,39] Fiorentino et al[8] showed that adults with NGT and 1-hr high (1-hr PG ⩾ 155 mg/dL or 8.6 mmol/l) had higher FPG, 1- and 2-hr insulin levels compared to NGT and 1-hr low (1-hr PG ⩽ 155 mg/dL or 8.6 mmol/l). This suggests decreasing insulin sensitivity, with hyperinsulinemia indicating the ability to compensate for IR, even among those with NGT. Fintini et al validated the cut off of 155 mg/dL (8.6 mmol/l) in a recent study of 1038 overweight/obese child and adolescents. They showed that the prevalence of NGT-1 hr high (1-hr PG ⩾ 155 mg/dL or 8.6 mmol/l) was greater than IGT (10% vs 8.4%). *Individuals with NGT and 1-hr high, had higher FPG, 1 and 2-hr insulin levels compared to those with NGT 1-hr low. Their findings align with* Fiorentino et al[8] and Fintini et al.[22] Our study validated the cut off 155 mg/dL (8.6 mmol/l) which aligns with studies by Fintini et al[22] and Tfayli et al.[25]

When we compare our cohort to that of Fintini et al, our subjects were older (13 years vs 11.8 years) and had higher BMI (34.7 vs 29.6-33.5). Fintini et al[22] suggested that prospective pediatric studies, as in adults, would likely demonstrate conversion rates may be two to threefold higher in those with IGT and high 1-hr PG than in isolated IGT. Manco et al validated in 2 cohorts (920-training sample and 534-validation sample; 52% boys, aged 2-18 years) that the 132.5 mg/dL (7.4 mmol/l) 1-hr cutoff versus 155 mg/dL (8.6 mmol/l) provided a sensitivity of 80.8% with a positive predictive value of 15.7%. This value correlated with the 1-hr PG predicting IGT (AUC 0.855, $P < .0001$) more accurately than FPG (AUC 0.637, $P = .001$). The cutoff value of 1-hr PG ⩾ 132.5 mg/dL (7.4 mmol/l) also was able to identify those with IGT with a sensitivity 80.8% and specificity 74.3%.[24] Marcovecchio et al[40] showed that in overweight/obese Caucasian NGT youth (age 11.1 + 2.7 years), the cut-off of 132.5 mg/dL (7.4 mmol/l) predicted lower insulin sensitivity (WBISI) and insulin secretion (Disposition Index).

Tricò et al[26] studied a multiethnic cohort of 202 adolescents (33% White; 31% Hispanic and 32% AA) comparing baseline to 2 years follow-up OGTT. As a group, the progression to prediabetes in those with NGT and 1-hr high (1-hr PG ⩾ 132.5 mg/dL [7.4 mmol/l]) was 3 times higher than in the NGT 1-hr low group (1-hr PG ⩽ 132.5 mg/dL [7.4 mmol/l]). (19.3% vs 7.6%, respectively) independent of age, sex, race/ethnicity, insulin sensitivity, and PG concentrations.

Manco et al[24] investigated a homogenous cohort of Caucasian youth who were younger, less heavy and less insulin resistant than our multiethnic cohort (10-11 years vs 13.9 years; BMI 28-32 vs 32.2; HOMA-IR 2.2-6.7 vs 4.5, respectively). The sensitivity of the 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) for predicting AGT in our study compared favorably with the sensitivity of 80% reported MAnco et al. Tricò et al[26] also studied a multiethnic cohort although there were differences in the ethnicity, age and pubertal staging in our subjects compared to the Trico cohort (Trico vs ours: 31% Hispanic vs 60%; age 12.3 years vs 13.9 years, Tanner IV-V: 34% vs 50%). This could explain why the 132.5 mg/dL (7.4 mmol/l) threshold in the Trico et al study differed in contrast to the 155 mg/dL (8.6 mmol/l) threshold in our cohort based on receiver operator curves.

Kim et al circumvented the limitations of cross-sectional studies with a longitudinal, natural history called **S**tudy **o**f **L**atino **A**dolescents at Risk (SOLAR) for T2D. Two hundred and thirty three Latino adolescents (mean age = 11.1) were followed for a mean of 4.7 ± 2.7 years. Using the cut-point of 155 mg/dL (8.6 mmol/l), the adolescents were divided into 2 groups and followed using OGTT and frequently sampled intravenous glucose tolerance test (FSIVGTT).[35] β-cell function measured by the Disposition Index (DI) declined by 58% in subjects with 1 hour PG ⩾ 155 mg/dL (8.6 mmol/l). In those with NGT and 1 hour PG ⩾ 155 mg/dL (8.6 mmol/l), there was a 2.54 odds ratio of progression to prediabetes during the 8-year follow-up. These results were independent of age, Tanner stage, fat mass, fasting, and 2-hr PG. This pediatric study, the first of its kind, highlighted that this specific value of the 1-hr PG in high-risk Latino children predicted progression to diabetes independent of other risk factors.[35] Furthermore, when using the cut off proposed by Manco et al of 132.5 mg/dL (7.4 mmol/l), there were no increased odds of developing prediabetes. Our study was a cross-sectional design with a population of predominantly Hispanic children (63%) who were older that those in the Kim et al study (14.2 ± 2.9 years vs 11.1 years) and heavier (BMI 32 vs 29). Similar to Kim et al, we plan to prospectively study the trajectory in the development of T2D in our ethnically diverse cohort. Our goal is to compare our findings with the pediatric studies mentioned above and clarify an ideal cut off for the 1-hr PG for future use.

Our cohort was predominantly Latino (>64%) and older which could affect the generalizability of our results. The retrospective review of our analysis is a potential limitation although there is an ongoing prospective study of high-risk groups (NGT_1-hr high, IGT, IFG and combined IFG + IGT) in progress. Furthermore, we recognize that the population studied included patients referred to this specialty clinic for prediabetes and T2D with preexisting metabolic complications (ie, PCOS, HTN). Thus they represent a pre-selected, high risk group, which might influence the population to which these results are extrapolated. Even though there is an abundance of literature comparing 1 and 2-hr PG in large and various populations including youth, we recognize that since 1-hr PG is measured during the same OGTT as the gold standard measures used to categorize AGT, there is potential for overestimation of the predictive potential of 1-hr PG in our ROC analysis.

Conclusion

In our multi-ethnic study, we found that the 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) provides information along the spectrum of glucose dysregulation beyond the FPG and 2-hr PG. The predictive value of 1-hr PG ⩾ 155 mg/dL (8.6 mmol/l) was almost as reliable as a 2 hours-PG, which makes a strong argument to consider performing the 1-hr PG during an OGTT in high-risk adolescents. Furthermore, the 1-hr PG is integral to our current understanding of the β-cell function and insulin sensitivity. There is a trajectory between prediabetes and T2D and this is accelerated in high risk children and adolescents. We have shown that the 1-hr PG provides a unique opportunity to identify those with NGT who have declining β-cell function. The 1-hr PG will increase the numbers of those with prediabetes, and is likely more predictive of progression, than 2-hr PG and HbA1. While we recognize that the precise threshold for the 1-hr PG value still requires further investigation, our threshold aligns with previous adult and pediatric studies. Of importance, the 1-hr PG adds considerably in predicting risk for progression to T2D, micro – and macro vascular disease and mortality[38,41,42] and therefore serves as an invaluable tool for identifying high-risk individuals who may benefit from aggressive lifestyle intervention and close monitoring.

We agree with the recent petition by Bergman et al[42] to consider a 1 hour OGTT to screen for prediabetes and a 2 hours OGTT and/or HbA1c measurement for diagnosis of T2D. More recently, a meta- analysis Ahuja et al[43] made an argument to reduce the duration of the OGTT to 1 hour for diagnosis of T2D at a value of 209 mg/dL (11.6 mmol/l). In addition, shortening the OGTT to 1-hour will likely facilitate its acceptance in clinical practice.[13]

In conclusion, our study has contributed to the current pediatric literature, supporting the 1-hr PG measurement during an OGTT, as it adds unequivocal value to our understanding of glucose dynamics along the spectrum from NGT to T2D, especially in multiethnic high risk children and adolescents.

Declarations

Ethics Approval and Consent to Participate
Not applicable

Consent for Publication
Not applicable

Author Contribution(s)
Preneet Cheema Brar: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing. **Shilpa Mehta:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing. **Ajay Brar:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Writing—original draft; Writing—review & editing. **Kristyn A Pierce:** Formal analysis; Methodology; Validation; Writing—review & editing. **Alesandro Albano:** Formal analysis; Investigation; Methodology; Project administration; Writing—review & editing. **Michael Bergman:** Formal analysis; Investigation; Methodology; Validation; Writing—original draft; Writing—review & editing.

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