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Is A1C Less Concordant with OGTT in Children as Compared in Adults? Data from a Hispanic Community in Arizona

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Abstract

Early efforts to identify hyperglycemia and those at risk for developing type 2 diabetes (T2DM) are warranted. For decades, the diagnosis of T2DM has been based on plasma glucose (PG) criteria but recent recommendations include the use of A1C for identifying hyperglycemia. These recommendations are based upon adult studies and data suggests that A1C may be less concordant in children, as compared to adults. The purpose of our study was to compare A1C, fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT) between adolescents and adults in Hispanic population at disproportionate risk for developing T2DM.

Methods: Data from self-identified as Latino, 91 overweight adolescents, and 406 overweight adults were assessed after an overnight fast for A1C, FPG and OGTT results. Receiver Operator Characteristics Curves for A1C vs. any hyperglycemia (prediabetes or diabetes) were then developed.

Result: 26 (28.6%) of the adolescents and 209 (51.5%) of adults exhibited hyperglycemia according to FPG and/OGTT. The prevalence of hyperglycemia as defined by an A1C>5.7% was 30.8% in adolescents and 55.6% in adults. Of the 26 adolescents, hyperglycemic on FPG and /or OGTT only 9 had A1C>5.7% for a sensitivity of 34.6%. This in contrast to adults, where the sensitivity of A1C>5.7% was 74.2%. Positive predictive value (PPV) for the A1C threshold of 5.7% was 32.1% in adolescents vs. 73.7% in adults.

Conclusion: Concordance of A1C with other measures of hyperglycemia is lower in overweight Hispanic adolescents, as compared to overweight Hispanic adults.

Keywords: Type 2 diabetes; Metformin; Prediabetes; Hyperglycemic

Abbreviations: T2DM: Type 2 Diabetes Mellitus; FPG: Fasting Plasma Glucose; OGTT: Oral Glucose Tolerance Test; ADA: American Diabetes Association; A1C: Hemoglobin A1C; DPP: Diabetes Prevention Program; ROC: Receiver Operator Characteristic Curves; PPV: Positive Predictive Value; NPV: Negative Predictive Value; PG: Plasma Glucose

Background

The diagnosis of Type 2 Diabetes (T2DM) has been based on criteria for fasting plasma glucose (FPG) or 2 hour glucose on an oral glucose tolerance test (OGTT); more recent recommendations from the American Diabetes Association (ADA) include the use of hemoglobin A1C (A1C) for identifying hyperglycemia [1]. Recent data suggest that A1C may be less concordant with FPG and OGTT in children, as compared to adults [2,3]. We acknowledge that concordance studies do not answer larger questions about long-term risks associated with hyperglycemia. Nonetheless, the issue is relevant because many pediatric subspecialty centers have taken to treating 'prediabetes' with metformin in many cases in adolescents, on the basis of the Diabetes Prevention Program (DPP) results in adults [4]. Also, there is a more established practice of treating T2DM in children with metformin and insulin [5]. Data on concordance allows subspecialty centers to determine how to utilize A1C in their treatment algorithms, if at all. The purpose of our study was to compare A1C, FPG, and OGTT between adolescents and adults in a Hispanic population at disproportionate risk for developing T2DM.

Methods

In participants self-identified as Latino, 91 overweight adolescents, and 406 overweight adults were assessed after an overnight fast for A1C, FPG, and OGTT results. All subjects were Latino in this population. Any subjects on medication for hyperglycemia were excluded, along with any subjects who identified themselves as having been previously diagnosed with diabetes or prediabetes. Other exclusions, such as hypertension, were not applied as the goal was to emulate a typical high volume clinic setting in which a variety of patients must be screened for diabetes. Inclusion criteria were Hispanic race, and overweight or obese status. Overweight or obese status for those age 10 to 20 was defined as BMI percentile ≥ 85th. For those ≥ 21 years, overweight or obese status was defined as a BMI > 25 kg/m^2 [6].

Prediabetes was defined as FPG ≥ 100 mg/dl, or 2 hour result on OGTT ≥ 140 mg/dl; diabetes was defined as FPG ≥ 126 or 2 hour result on OGTT ≥ 200. Initial analysis at the A1C threshold of 5.7% was performed, to determine correlation between the A1c threshold of 5.7% and presence or absence of hyperglycemia on FPG or OGTT. Receiver Operator Characteristics curves (ROC) for A1C vs. any

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hyperglycemia (prediabetes or diabetes) were then developed, to determine whether other A1c thresholds resulted in greater correlation with other measures of hyperglycemia.

Results

26 (28.6%) of the adolescents and 209 (51.5%) of adults exhibited hyperglycemia according to FPG and/or OGTT. The prevalence of hyperglycemia as defined by an A1C ≥ 5.7% was 30.8% in adolescents and 55.6% in adults. However, despite similar percentages in the number of subjects defined as hyperglycemic, there was poor agreement between the tests for identifying hyperglycemic adolescents. Of the 26 adolescents hyperglycemic on FPG and/or OGTT only 9 had A1C ≥ 5.7%, for a sensitivity of 34.6%. This is in contrast to adults, where the sensitivity of A1C ≥ 5.7% was 74.2%. Similarly, positive predictive value (PPV) for the A1C threshold of 5.7% was 32.1% in adolescents vs. 73.7% in adults.

A1C's performance marginally improved as a 'rule-out' test in adolescents, as of the 63 adolescents with an A1C <5.7%, 46 were not hyperglycemic by FPG or 2HrPG (Specificity=70.8%). Of the 181 adults with an A1C<5.7%, 127 did not exhibit elevated FPG or 2HrPG (Specificity=64.5%). Similarly, negative predictive value (NPV) for the A1C threshold of 5.7% was 73.7% in adolescents and 70.2% in adults.

5.7% is the recommended ADA threshold for prediabetes in adults, and the threshold at which most laboratories will report an 'abnormal' to the provider. Since correlation at this point was poor, we sought to define at what point correlation was better, by developing ROC curves for A1C vs. any hyperglycemia (prediabetes or diabetes).

As shown in the ROC curve and table (Figure 1 and Table 1), for overweight adolescents, using the presence of any hyperglycemia on FPG or OGTT as a de-facto gold standard, lower A1C values, such as 5.45%, do raise sensitivity to more than 70%, however, specificity then declines to near 50%.

For overweight adults, the ROC curve and table (Figure 2 and Table 2) closely approximated the ADA recommendations, with values near 5.7% providing the best combination of sensitivity and specificity, when the presence of any hyperglycemia on FPG or OGTT is used as a de-facto gold standard.

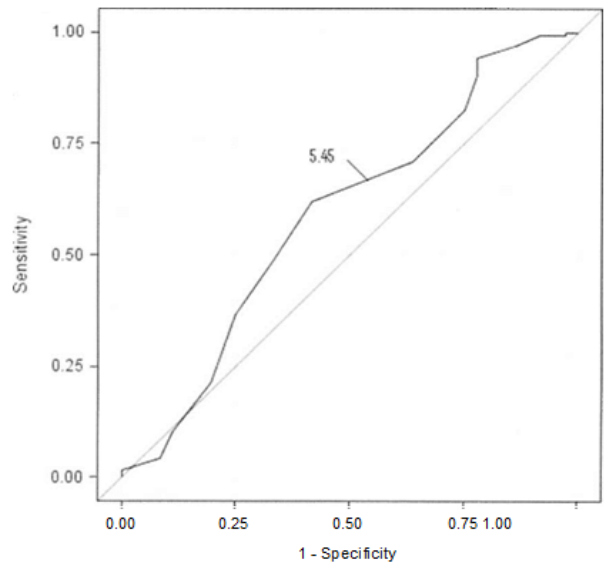

Figure 1: ROC Curve for Adolescents.

Hemoglobin A1C	Sensitivity	Specificity	Sum of Sensitivity and Specificity
5.05	0.923	0.062	0.985
5.15	0.885	0.138	1.023
5.25	0.808	0.215	1.023
5.35	0.769	0.338	1.107
5.45	0.731	0.508	1.239
5.55	0.615	0.585	1.2
5.65	0.346	0.708	1.054
5.75	0.231	0.815	1.046
5.85	0.192	0.908	1.1
5.95	0.192	0.938	1.13
6.05	0.115	0.985	1.1
6.15	0.038	1	1.038

Table 1: A1C vs sensitivity, specificity, and sum in overweight and obese adolescents.

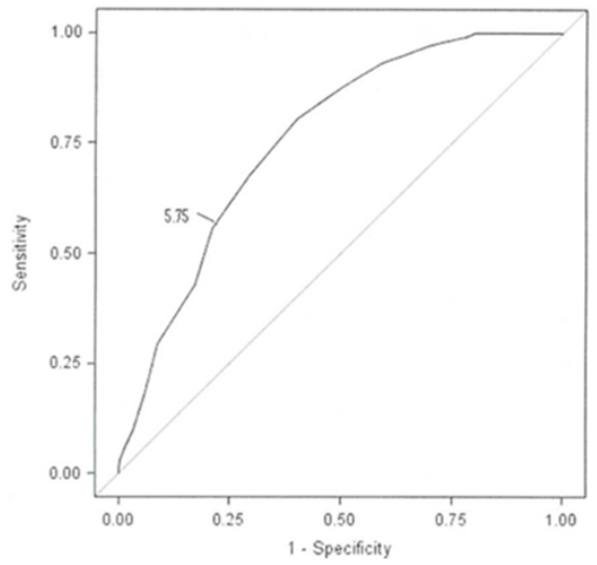

Figure 2: ROC Curve for Adults.

Hemoglobin A1C	Sensitivity	Specificity	Sum of Sensitivity and Specificity
5.05	0.986	0.051	1.037
5.15	0.971	0.091	1.062
5.25	0.952	0.162	1.114
5.35	0.923	0.259	1.182
5.45	0.852	0.391	1.243
5.55	0.823	0.528	1.351
5.65	0.742	0.645	1.387
5.75	0.627	0.782	1.409
5.85	0.517	0.853	1.37
5.95	0.426	0.914	1.34
6.05	0.359	0.944	1.303
6.15	0.316	0.964	1.28
6.25	0.297	0.97	1.267
6.35	0.244	0.985	1.229
6.45	0.23	0.99	1.22
6.55	0.206	1	1.206

Table 2: A1Cvs sensitivity, specificity, and sum in overweight and obese adults.

Of note, in this study, there were no cases of diabetes in the obese adolescent population by FPG or OGTT, so all of the identified hyperglycemia was 'prediabetes'. There were 53 total cases of diabetes on FPG or OGTT in obese adults, and A1C was ≥ 5.7% in 51 of them.

Conclusions

In the overweight adult population, our correlation results closely approximate the recommendations put forth by the ADA.

In the overweight adolescent population, thresholds of A1C to provide high concordance with FPG or OGTT are more difficult to identify.

Overall, we conclude that concordance of A1C with other measures of hyperglycemia is lower in overweight Hispanic adolescents, as compared to overweight Hispanic adults. Also, we conclude that for pediatric specialty clinics that have determined that clinical protocol is to treat 'pre-diabetes' as diagnosed on FPG or OGTT in adolescents with metformin, A1C does not offer additional guidance.

However, we do note that A1C is as good as FPG or OGTT, in adults, for identifying long-term complication risk, and that no similar studies regarding long-term complication risk have been carried out in adolescents or children; Thus, concordance studies provide an incomplete picture [7,8]. A1C may yet prove useful in primary care or urgent care settings, where the goal, rather than identification of prediabetes, is likely to be rule-out of significant hyperglycemia and diabetes requiring immediate treatment.

Author's Contributions

MCH, CK, and GS obtained and evaluated the research data. MCH and CK wrote the manuscript. PG helped in statistical analysis. GS, MCH, DM, CK, and PG contributed to discussion, reviewed/edited manuscript.

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