RESPONSE TO COMMENT ON REDONDO ET AL.

Racial/Ethnic Minority Youth With Recent-Onset Type 1 Diabetes Have Poor Prognostic Factors. Diabetes Care 2018;41:1017–1024

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We thank Dr. Nwosu for his thoughtful comments (1). We agree that insulin resistance influences insulin dose–adjusted hemoglobin A_{1c} (IDAA1c). Nagl et al. (2) observed that the partial remission period was less frequent and shorter in girls than boys, but, without C-peptide measurements, the authors could only speculate that higher insulin resistance or lower insulin secretion might explain their findings. However, we found that, adjusting for BMI, age, and sex, insulin doses were still different between African Americans (AAs) and non-Hispanic whites (NHWs) ($P < 0.001$) (3), suggesting that after controlling for factors that increase insulin resistance there was still a difference in insulin dose, and thus in IDAA1c. Other measures of partial remission period, e.g., insulin dose, are also affected by insulin resistance. Furthermore, although defining partial remission period based on absolute threshold of insulin secretion, as measured by C-peptide, may work well in lean, white children, the same level of insulin secretion may be insufficient in the setting of insulin resistance induced by older age, puberty, female sex, or race. Therefore, measures of partial remission period that are influenced by insulin resistance, such as IDAA1c, may better reflect sufficiency of residual insulin secretion than an absolute C-peptide value. We agree that IDAA1c also is influenced by vagaries in determination of insulin dose (e.g., self-reported insulin dose may be uncertain), which could result in misestimating insulin secretion. Overall, we agree with Nwosu (1) on the advantages of developing and validating IDAA1c thresholds for different races and ethnicities, sex, age, pubertal stage, weight, and other influential characteristics, although the use of multiple cut points may prove difficult to integrate in analyses.

We acknowledged that AAs have higher HbA_{1c} than whites for the same mean glucose concentrations (4). Of note, the observed differences in IDAA1c between NHWs and AAs were larger, particularly at 6 and 12 months (1.8% and 1.7%, adjusted for age and sex) (3) than expected based on the race-related difference in HbA_{1c} of 0.4% (4). If this 0.4% "correction" is applied to our data, differences between NHW and AA children at 6 and 12 months are reduced (1.4% and 1.3%) but still significantly different ($P < 0.001$) at both time points. Furthermore, although HbA_{1c} difference increased between 6 and 36 months, the difference in IDAA1c was largest at 6 months and progressively decreased at 12, 24, and 36 months. This observation supports that the presence or absence of partial remission period during the first year after onset explains a considerable part of IDAA1c differences, and as partial remission period rarely persists in all groups beyond the first year, IDAA1c values become more similar.

As AAs have better lipid profiles at similar degrees of adiposity than NHWs (5), their similar dyslipidemia frequencies could in fact reflect worse glycemia in AAs.

Finally, we agree with Nwosu's conclusion that more funding is needed to develop and validate a definition of partial remission period in nonwhite races and ethnicities. We hope that our article has highlighted additional racial/ethnic differences that warrant further research.

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References

1. Nwosu BU. Comment on Redondo et al. Racial/ethnic minority youth with recent-onset type 1 diabetes have poor prognostic factors. Diabetes Care 2018;41:1017–1024 (Letter). Diabetes Care 2018;41:e123–e124. DOI: 10.2337/dc18-0483

2. Nagl K, Hermann JM, Plamper M, et al. Factors contributing to partial remission in type 1 diabetes: analysis based on the insulin dose-adjusted HbA1c in 3657 children and adolescents from Germany and Austria. Pediatr Diabetes 2017;18:428–434

3. Redondo MJ, Libman I, Cheng P, et al.; Pediatric Diabetes Consortium. Racial/ethnic minority youth with recent-onset type 1 diabetes have poor prognostic factors. Diabetes Care 2018;41:1017–1024

4. Bergenstal RM, Gal RL, Connor CG, et al.; T1D Exchange Racial Differences Study Group. Racial differences in the relationship of glucose concentrations and hemoglobin A_{1c} levels. Ann Intern Med 2017;167:95–102

5. Bacha F, Saad R, Gungor N, Janosky J, Arslanian SA. Obesity, regional fat distribution, and syndrome X in obese black versus white adolescents: race differential in diabetogenic and atherogenic risk factors. J Clin Endocrinol Metab 2003;88:2534–2540