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Factors Affecting Hemoglobin A1C in the Diagnosis of Diabetes and Prediabetes in Youth

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Purpose We sought to examine the correlation between variables and A1C levels to determine if prediction modeling could be used in the screening and diagnosis of diabetes and prediabetes in youth. We also sought to test relationships between A1C levels to insulin sensitivity indices and β-cell function indices.
Design and methods: We performed a retrospective review of 904 medical records from youth deemed at-risk for the disease. We performed Pearson correlation, multiple regression, and simple regression testing to determine the relationship between variables and A1C levels. In addition, we performed Pearson correlation testing on insulin sensitivity indices and β-cell function indices to determine the strength of correlation to A1C levels.
Results: Statistical analysis did not show a strong relationship between the variables tested and the A1C. When racial and ethnic groups were tested together, the results from African American participants resulted in bias estimates, and as a result, a statistical model for the entire sample could not be performed. Results indicate that A1C is correlated with all β-cell function proxy measurements and correlated to the corrected insulin level at 30 minutes, but not the fasting insulin or insulinogenic index.
Discussion: The results from this study underline the multi-dimensional causes of diabetes and prediabetes and further stress the difficulties in predicting the diseases. The causes of diabetes and prediabetes are multifaceted, often individualized, and often difficult to ascertain.
Practice implications: Clinicians should continue to examine a variety of variables prior to determining the need for diabetes diagnostic testing.

THE AMERICAN DIABETES Association currently recommends screening for type 2 diabetes in asymptomatic adolescents, if their BMI is greater or equal to the 85% percentile, and the adolescent has 2 or more risk factors for the disease. Risk factors can include family history, at-risk racial/ethnic group, conditions or signs of insulin resistance, small for gestational age at birth, or maternal history of gestational diabetes. The ADA further recommends screening tests be limited to FPG, due to cost and convenience (ADA, 2014). The International Diabetes Federation has yet to endorse the use of A1C testing for adolescents or children, although it has endorsed its use for adults (Nowicka et al., 2011). There is a paucity of research regarding the clinical utility of A1C to predict diabetes and prediabetes in children and adolescents.

The correlation between plasma glucose and A1C also has been shown to differ between adults and youth. Ogawa et al. (2012) examined school-aged children in Japan (N = 298) and found FPG levels were not as highly correlated to A1C, when compared to adult counterparts. Seino et al. (2010) found similar results in school-age children group, with an A1C of 6.5% correlated to a FPG = 111.4 mg/dL, Similar

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research shows standardized scales correlating A1C to plasma glucose concentrations should be reanalyzed for children and adolescents.

Research has yet to consistently examine the effects of various factors on A1C in children and adolescence. As noted in Figure 1, a variety of factors influence glycemic control and subsequently A1C. This study will examine BMI, race/ethnicity, age, gender, insulin sensitivity, beta cell (β-cell) function to determine their influence on A1C. While it is widely accepted that β-cell dysfunction is a known contributor to increased A1C, the contribution of various factors to the A1C in children and adolescents has not been fully explored. A traditional literature review was performed to address factors influencing A1C in children and adolescents and to identify further gaps in the literature with regard to these factors.

Racial and Ethnic Factors

Racial and ethnic groups show statistically significant mean differences and variation in A1C (Herman et al., 2007, 2009; Kirk et al., 2008). Studies have shown variations in A1C among different racial groups, whereas mean plasma glucose concentrations do not vary between racial groups. These results suggest a biological basis for the variability across racial groups with respect to A1C testing (Bonds et al., 2003; Christensen et al., 2010; Cohen, 2007).

Kirk et al. (2005) concluded that the differences between racial and ethnic groups were consistent across previous research studies, after adjusting for covariates. Herman et al. (2007) also compared A1C from 5 different racial and ethnic groups. Using an adult sample (N = 3,819), the study found that A1C was higher in racial and ethnic minority after adjusting for other covariates. The difference was particularly high among African American and Hispanic subjects. Herman et al. (2007) concluded caution should be taken when using A1C to diagnose diabetes in certain minority groups.

Herman et al. (2009) further examined the racial and ethnic difference in A1C when compared to mean plasma glucose concentrations. Using a multicenter sample in 11 countries (N = 2094), the study found difference between racial and ethnic groups for A1C and 1,5-anhdroglucitol levels, but not for mean plasma glucose concentrations. The research suggests that criteria established for the diagnosis of diabetes based on A1C might be challenging due to inherent differences between racial and ethnic groups (Herman et al., 2009).

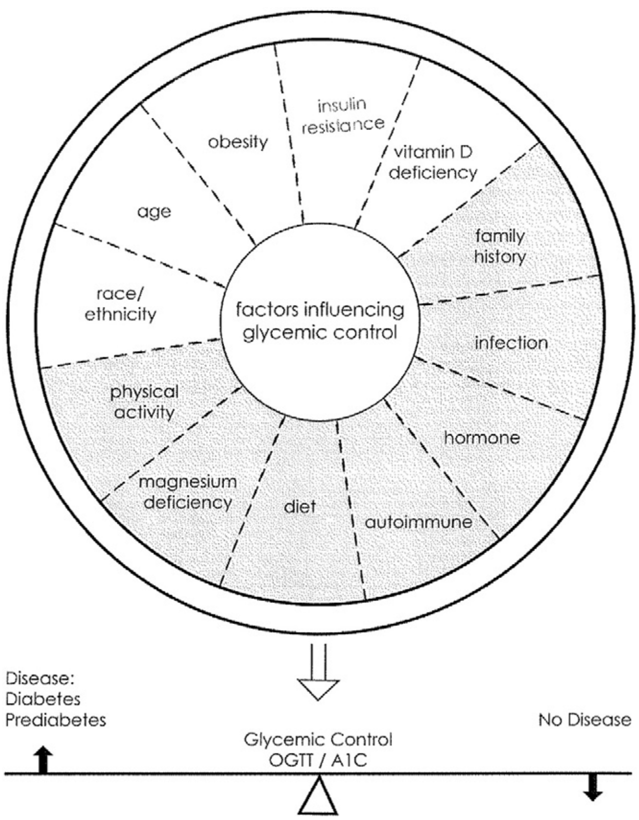

Figure 1 Concept map illustrating glycemic control.

BMI and Lifestyle

Research has supported the concept that multiple metabolic, physiological, and lifestyle factors exist that influence serum glucose and A1C (Maruther et al., 2011). Research also has identified factors that explain the difference in A1C between racial and ethnic groups that include lifestyle choices and health disparities (Maruther et al., 2011). Most research focuses on lifestyle choices, such as diet and exercise, and their impact on glucose concentrations. Obesity is a known risk factor for the development of diabetes and prediabetes in children and adolescents, as a positive correlation is seen between BMI and the presence of the disease (ADA, 2014). However, little research has focused on the effects of diet and exercise directly on the A1C.

Age

Little research exists that examines factors influencing A1C in children or adolescents. Cho, Craig, and Donaghue (2014) determined puberty marked a significant shift in glycemic control and diabetes complications. As the start of puberty varies between individuals, it is difficult to ascertain when puberty and age begin to affect glycemic control for an individual. Mortenson & Hougaard also noted that individuals with earlier onsets of puberty have an increased risk for developing prediabetes or diabetes. As the onset of puberty grows increasingly earlier, due to diet and activity levels, age should be evaluated as a possible proxy to the onset of puberty and the possible risk of disease development.

Vitamin D Deficiency

Recent research has focused on the role of Vitamin D in diabetes (Takiishi, Gyseman, Bouillon, & Mathieu, 2010). Vitamin D deficiency has a suspected role in the development of type 1 diabetes and in the functional ability of β-cells in type 2 diabetes (Zitterman, 2003). According to Yiu et al. (2011), there is a significant correlation between vitamin D