Are Hemoglobin Levels Elevated in Type 1 Diabetes?

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OBJECTIVE — While lower hemoglobin is generally associated with adverse events in diabetes, we have recently observed in type 1 diabetes that those with overt nephropathy had hemoglobin levels as high as 18.8 g/dl. We thus explored whether hemoglobin concentrations are generally higher in type 1 diabetes.

RESEARCH DESIGN AND METHODS — Baseline (1986–1988) hemoglobin levels from the Pittsburgh Epidemiology of Diabetes Complications Study (EDC) of type 1 diabetes were compared with general population data from the National Health and Nutrition Examination Survey (NHANES) III in the same age range as the EDC population (aged 8–48 years).

RESULTS — Both male and female EDC study participants had significantly higher hemoglobin levels than their NHANES III counterparts (men: 16.0 vs. 15.1 g/dl, P < 0.0001; women: 14.1 vs. 13.3 g/dl, P < 0.0001). The difference between the two populations was greatest in adolescent female subjects.

CONCLUSIONS — Hemoglobin levels may be higher in type 1 diabetes than in the general population, which may have important clinical implications.

Although low hemoglobin is generally associated with adverse events in diabetes (1) and kidney disease (2), we have recently observed relatively high hemoglobin levels (as high as 18.8 g/dl) among individuals with type 1 diabetes and overt nephropathy (3) compared with the general renal disease population (4). This led us to question whether hemoglobin levels are generally higher in type 1 diabetes.
tus was less marked. Women without overt nephropathy still showed this age-related decline, and the difference by overt nephropathy status did not reach statistical significance until age 40 years (online appendix Fig. 1 [available at http://care.diabetesjournals.org/cgi/content/full/dc09-0713/DC1]).

To determine whether the elevated hemoglobin observed in EDC subjects might simply be due to increased hemoconcentration from dehydration secondary to poor glycemic control, analyses were repeated with EDC participants restricted to those with 1) A1C levels greater than or equal to the median and 2) A1C levels less than or equal to the median. Similar results were obtained to those in Fig. 1.

In a subanalysis, hemoglobin levels in our 13 African American female subjects with type 1 diabetes (aged 18–39 years) did not differ from our Caucasian female subjects (13.7 vs. 14.1 g/dl, P = 0.20) but were significantly higher than NHANES III African American female subjects (13.7 vs. 12.4 g/dl, P < 0.0001). Hemoglobin levels significantly differed between NHANES III African American and Caucasian female subjects (12.4 vs. 13.2 g/dl, P < 0.0001). Sample size prohibited formal analyses in males.

**CONCLUSIONS** — We have demonstrated that hemoglobin levels are higher in type 1 diabetes than in the general population, by ≈1 g/dl. To our knowledge, this is the first report to document this finding. We have shown that this difference is greatest for adolescent females, particularly striking since in the general population the adolescent rise in hemoglobin is only observed in male subjects (8). Although hemoglobin levels began to decline in type 1 diabetes in the early to mid-20s this decline was not observed in the general population. In men with type 1 diabetes, kidney disease largely accounted for this decline. The increase in hemoglobin was unrelated to glycemic control.

Potential explanations include a response to generalized hypoxia secondary to vascular disease, or a response to testosterone, which has been reported to be increased in type 1 diabetes (9,10). In addition to the erythropoietic effects of testosterone, insulin and insulin-like growth factor-1 and -2 stimulate erythropoietin production in astrocytes (11). Finally, intermittent ketosis might lead to increased β-hydroxy-butyrate, resulting in higher fetal hemoglobin (12) and hence total hemoglobin levels. Elevated fetal hemoglobin has been observed in both children and adults with type 1 diabetes and correlated only weakly (13), or not at all (14), with glycemic control but increased in adolescence (14). These data have potentially important clinical implications not only for interpreting hemoglobin values in type 1 diabetes but also for complications, as we have recently reported that high hemoglobin is a risk factor for proliferative retinopathy in men; while in women, who are more likely to be in the normal to low end of the hemoglobin distribution, a U-shaped relationship exists (15).

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