

HbA_{1c} increases with age

Original article:

Effect of aging on A_{1c} levels in individuals without diabetes: evidence from the Framingham Offspring Study and the National Health and Nutrition Examination Survey 2001–2004. Pani LN, Korenda L, Meigs JB, Driver C, Chamany S, Fox CS, Sullivan L, D'Agostino RB, Nathan DM. *Diabetes Care* 2008; 31(10): 1991–6.

Summary and Comment:

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Key words:

HbA_{1c}, age, glycemic control, treatment goals

Summary

Although glycemic levels are known to rise with normal ageing, the non-diabetic HbA_{1c} range is not age-specific. The authors studied whether HbA_{1c} is associated with age in non-diabetic subjects and in subjects with normal glucose tolerance (NGT) in two population-based cohorts. Cross-sectional analyses of HbA_{1c} were carried out across age categories in 2473 non-diabetic participants in the Framingham Offspring Study [1] and in 3270 non-diabetic participants in the National Health and Nutrition Examination Survey (NHANES) 2001–2004 [2]. In the Framingham Offspring Study, HbA_{1c} was examined by age in a subset of subjects with NGT, i.e. after excluding those with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT). Multivariate analyses were performed, adjusting for sex, BMI, fasting glucose and 2-h postload glucose values.

The authors found that HbA_{1c} levels were positively associated with age in non-diabetic subjects (Fig. 1). Linear regression revealed 0.014 and 0.010 percent increases in HbA_{1c} per year in the non-diabetic Framingham and NHANES populations, respectively. The 97.5th percentiles for HbA_{1c} were 6.0% and 5.6% for non-diabetic individuals aged <40 years in Framingham and NHANES, respectively, compared with 6.6% and 6.2% for individuals aged >70 years (*p* for trend <0.001). The association of HbA_{1c} with age was similar when restricted to the subset of Framingham subjects with NGT and after adjustments for sex, BMI, fasting glucose and 2-h postload glucose values.

It was concluded that HbA_{1c} levels are positively associated with age in non-diabetic populations even after exclusion of subjects with IFG and/or IGT, and that further studies are needed to determine whether age-specific diagnostic and treatment criteria would be appropriate.

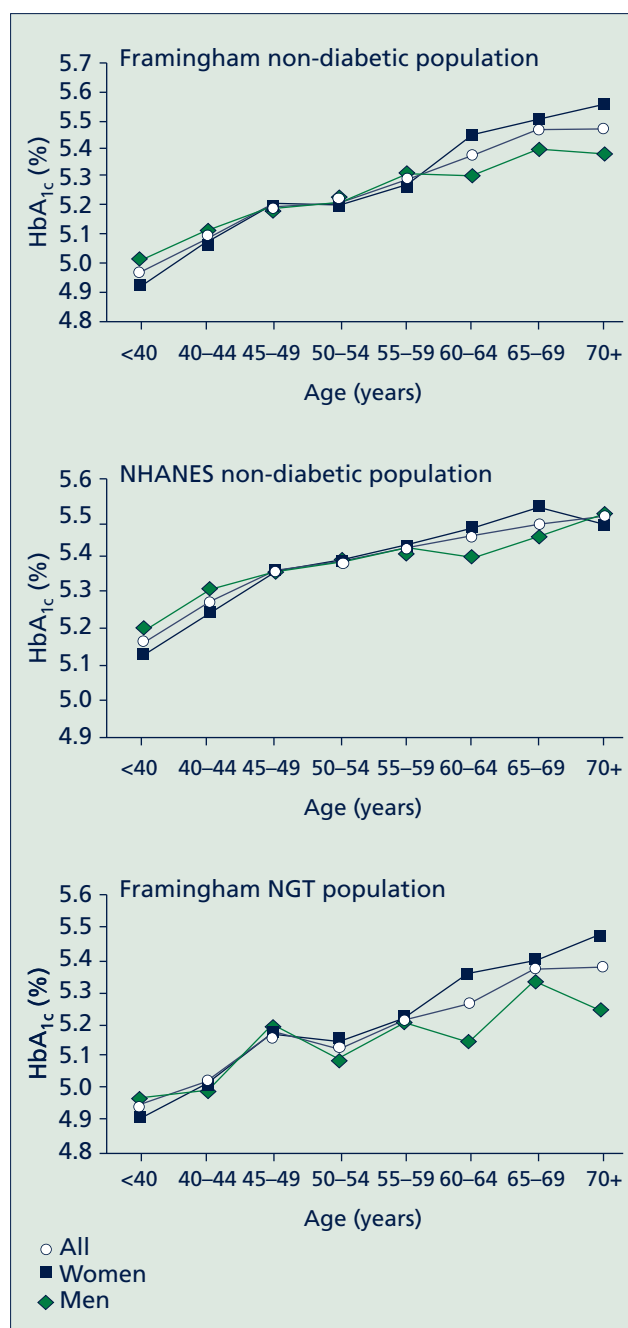


Fig. 1: Mean HbA_{1c} by age categories in the Framingham non-diabetic population (top), the NHANES 2001–2004 non-diabetic population (middle) and the Framingham NGT population (bottom). Tests for trend were significant at *p* < 0.0001 for both the Framingham and NHANES populations.

Comment

What could cause HbA_{1c} levels to increase with age? There are several possibilities.

- Increased HbA_{1c} is most likely due to the slightly higher blood glucose levels found in elderly people, even within what is considered normal values.
- Another possible cause could be that erythrocyte survival is somewhat prolonged in the elderly, maybe due to reduced physical activity.
- Some substances facilitate or impede the glycation of proteins. Changes in eating habits

may therefore have an effect on the glycation of hemoglobin and other extracellular proteins.

- There is a well-known decrease in glomerular filtration rate with age, and renal failure is associated with increased HbA_{1c} levels.

It is well documented that there is a direct relationship between HbA_{1c} and the risk of cardiovascular disease even at normal HbA_{1c} values [3]. Similarly, higher fasting blood glucose in the normal range is also associated with increased mortality [4]. It has recently been proposed that HbA_{1c} determination might be used for screening and diagnosing diabetes [5]. The small effects of age on HbA_{1c} should be taken into consideration in this discussion but should not be of paramount concern.

HbA_{1c} levels increase with age by about 0.01–0.014% per year. Thus the upper normal range increases by between 0.2% and 0.3% between the ages of 50 and 80, or, as stated in the study: ‘The 97.5th percentiles for HbA_{1c} were 6.0% and 5.6% for non-diabetic individuals aged <40 years in the Framingham Offspring Study and NHANES, respectively, compared with 6.6% and 6.2% for individuals aged >70 years.’ It may be useful to remember this. Most of us, however, would probably be a little more flexible in our treatment goals in the elderly or in those with limited life expectancy from other

causes. The American Diabetes Association recommendations have commented wisely upon this: ‘Less stringent HbA_{1c} goals may be appropriate for patients with a history of severe hypoglycemia, patients with limited life expectancies, children, individuals with comorbid conditions, and those with longstanding diabetes and minimal or stable microvascular complications’ [6].

References

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