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Glycosylated hemoglobin (HbA1c): A Biomarker of Anti Aging

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ABSTRACT

Glycosylated hemoglobin (HbA1c) is a marker of evaluation of long-term glycemic control in diabetic patients that predict risks for the development and progression of diabetic complications. The aim of this study is to evaluate the significance of Glycosylated hemoglobin (HbA1c) in relation to aging. After going through number of research papers have come to conclusion that such relationship do exist and Glycosylated hemoglobin (HbA1c) does increase with advancing age independent of glycemia. It also clearly shows association with premature aging and increased mortality. Review Criteria: We systematically searched number of articles, webpages, and major textbooks for writing this article. All papers identified were in English language and full manuscripts. I also searched the reference lists of identified articles for additional relevant papers. A search for reference data for this purpose was also performed using the Google search engine. In this short review we summarize the findings given by different researchers on the subject and bring it in our support to prove HBA1C should also be used as anti aging tool.

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Introduction

Glycation

Aging is a multi dimensional process of becoming older and remains one of the most mysterious areas of biological research. It represents the accumulation of changes in a person over time [1][2].

It is among the largest known risk factors for most human diseases.[3] Roughly 100,000 people worldwide die each day of age-related causes.[4]

Since ageing is a cause or major risk factor of the age related diseases and mortality, there are growing efforts in ageing research to slow ageing and extend healthy lifespan. Ageing processes can be faster because of accumulation of toxic metabolic products.

These products could be rogue Advanced Glycation end products formed from reducing sugars such as glucose, that react non enzymatically with amino groups in proteins, lipids and nucleic acids through a series of reactions forming Schiff bases and Amadori products to produce AGE.

This process, also known as the Maillard reaction was described in the early 1900s, when it was noted that amino acids heated in presence of reducing sugars developed a characteristic yellow brown colour.[5]

These Advanced Glycation end products corrode our body the same way rust damages metal in a machine. AGEs as they build up in the body, they bombard the body's cells like a meteor shower and continue to cause more damage and rusting that becomes noticed over many years.

This Glycation, make cells stiffer, less pliable and subject to damage and premature aging. This is one reason why joints, muscles and tendons become stiff and inflexible over time. Glycation thus plays an important role in ageing and has been implicated in the pathophysiology of number of diseases

For most people with normal levels of glucose, the Glycation process is something that happens gradually over the course of a lifetime, and it's really not that big of a deal, However people with high sugar levels in body lead to quick and more formation of AGEs, that hastens damage to cells of body and early aging.

When you're younger, your body has more resources to ward off damage, and you're producing more collagen, says New York and Miami-based dermatologist Fredric Brandt, who in 2007 was one of the first to launch an anti-aging skin-care line specifically addressing glycation. When you reach a certain age, these Glycation products begin to build up at the same time that your threshold for damage is getting lower.

Glycation is a fact of life. It's happening right now, to all of us. It can even be measured. There are number of biomarkers shown to be related with the ageing process. One of these biomarkers is glycated hemoglobin (HbA1c). The A1C test is based on non-enzymatic Glycation pathway by hemoglobin's exposure to plasma glucose. Therefore Glycation measurement can give idea how fast it is happening in our body to lead to aging and various age related diseases.

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Hemoglobin A1C and aging

The hemoglobin A1C test also called HbA1c, glycated hemoglobin test, or glycohemoglobin test is an important blood test used to determine how well diabetes is being controlled. Hemoglobin A1C provides an average of blood sugar control over a six to 12 week period. [6]

However, the same blood test also helps identify age-accelerating Glycation reactions in the body. The hemoglobin A1C blood test is thus being considered as useful in non-diabetics who want to guard against the destructive Glycation process.

The hemoglobin A1C test identifies the potential for age-accelerating Glycation reactions in our bodies. However, this valuable tool has been dramatically underutilized in the context of aging.

Scientists believe that it is not only those with diabetes or pre-diabetes who should be concerned about the damaging effects of Glycation in the body, but all of us should be concerned as the damage inflicted by advanced Glycation end-products (AGEs) is more as the age advances.

Lydie N. Pani, Leslie Korenda and others published a research "Effect of Aging on A1C Levels in Individuals without Diabetes" they found that A1C was associated with age in nondiabetic subjects and in subjects with normal glucose tolerance (NGT) in two population-based cohorts. [7]

They performed cross-sectional analyses of A1C across age categories in 2,473 nondiabetic participants of the Framingham Offspring Study (FOS) and in 3,270 nondiabetic participants from the National Health and Nutrition Examination Survey (NHANES) 2001–2004. The results in their study showed positive association of A1C with age in nondiabetic subjects. The 97.5th percentiles for A1C were 6.0% and 5.6% for nondiabetic individuals aged <40 years in FOS and NHANES, respectively, compared with 6.6% and 6.2% for individuals aged =70 years.

They further concluded that the studies that have failed to demonstrate an association between age and A1C used diagnostic criteria to exclude diabetes that are now outdated or were small and possibly underpowered. [8–10]

In another study researchers concluded that Glycemic control deteriorates with age in healthy, non-diabetic individuals. Age-related rises in haemoglobin A1C result from a small but steady decline in pancreatic beta cell function. [11]

Similarly Frank Q. Nuttall, in the study found that there was a modest age-related increase in %HbA1c. [12]

While as in another study on Japanese Population showed the same results. This study on Japanese population was done to evaluate whether there is any change in HbA1c with age and to determine the effects of body mass index (BMI), exercise, and family history of diabetes on this change.

A cross-sectional survey of 7,664 male Japanese workers aged 20–59 years was performed. All subjects received a physical examination that included measurement of HbA1c as an indicator of plasma glucose level. The subjects were classified according to their ages and BMIs, and any relationship with HbA1c levels was evaluated. [13]

Results showed that in all BMI groups, HbA1c increased with age. The greatest increase in HbA1c was observed in the 40 to 49 year-old age-group in subjects with a BMI =26 kg/m² and in the 30 to 39 year old age group in subjects with a BMI >26.

HbA1c in the subjects aged 20 to 29 years did not change with BMI. In contrast, HbA1c in subjects aged 30 to 59 years was significantly higher in those with a BMI >26 when compared with those with BMI =20.

The age dependent increase in HbA1c was greater in subjects with a positive rather than negative family history of diabetes. They further concluded that the age dependent increase in HbA1c may be a consequence of the aging process itself. [13]

Therefore monitoring of hemoglobin A1c levels is essential for all adults who wish to identify excess glycation processes in their bodies and take measures to control and minimize glycation induced damage, as the favourable glucose metabolism and its control has been identified as a central key factor for longevity. [14]

A Community-based cross-sectional study involving 2368 subjects aged = 20 years was done from Chandigarh, India and all had normal glucose tolerance. In this study there was a significant positive correlation between mean HbA1c and age in these subjects.

The increase in HbA1c with each advancing year was 0.01% above the age of 20 years. A significantly higher number (6.5%, 21/325) of subjects had HbA1c of = 6.5% (48 mmol/mol) in those above the age of 50 years compared with those below the age of 50 years and it was concluded that HbA1c increases with advancing age independent of glycaemia. [15]

Conclusions

A1C levels are positively associated with age in nondiabetic populations. The age-dependent increase in HbA1c may be a consequence of the aging process itself independent of glycaemia. Age therefore should be taken into consideration when using HbA1c for the diagnosis and management of diabetes and prediabetes.

The HbA1C test which is being used primarily to monitor blood sugar control in diabetics also helps to identify the level of age-accelerating Glycation in our body.

Therefore being important factor in aging makes the hemoglobin HbA1C test important tool for anti aging program to prevent accelerated aging due to various problems.

HbA1C level is an indirect measure of how fast you are aging and how much damage is likely being done to your cells by the aging process.

Together with other key anti aging tests, the HbA1C blood test is a marker for potential accelerated aging, and can help to clear the problems and complications of high blood sugar and Glycation. Knowing your HbA1C levels and responding accordingly will ensure a much longer and healthier life

REFERENCES

1. Bowen, Richard L.; Atwood, Craig S. (2004). "Living and Dying for Sex". *Gerontology* 50 (5): 265–90. Doi: 10.1159/000079125. PMID 15331856 <http://agingresearch.wisc.edu/pdf/AGING%20THEORY.pdf>
2. Birbrair, A.; Zhang, T.; Wang, Z.-M.; Messi, M. L.; Mintz, A.; Delbono, O. (2013). "Type-1 pericytes participate in fibrous tissue deposition in aged skeletal muscle". *AJP: Cell Physiology* 305 (11): C1098. doi:10.1152/ajpcell.00171.2013. <http://ajpcell.physiology.org/content/ajpcell/305/11/C1098.full.pdf>

3. Dillin A, Gottschling DE, Nyström T; Gottschling; Nyström (2014). "The good and the bad of being connected: the integrons of aging". *Current Opinion in Cell Biology*: Volume 26, February 2014, Pages 107–112. doi:10.1016/j.ceb.2013.12.003. PMC 3927154. PMID 24529252. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3927154/>
4. De Grey, Aubrey D.N.J (2007). "Life Span Extension Research and Public Debate: Societal Considerations". *Studies in Ethics, Law, and Technology* 1doi:10.2202/1941-6008.1011 <http://www.sens.org/files/pdf/ENHANCE-PP.pdf>
5. R.Singh, A.Barden, T.Mori, L.Beilin,"Advanced glycation end products: a review", *Diabetologia* (2001)44:129-146 <http://agefoundation.com/wp-content/uploads/2013/01/SpringerBookArchivesStudy.pdf>
6. Raval DK, Shah H K, Meghani NM, Bhut VG," Hemoglobin A1C: biomarker for diabetes prediction?",*INTERNATIONAL JOURNAL OF PHARMACOLOGY AND THERAPEUTICS*, Issue 1 : 2011. <http://www.earthjournals.org/ijpt-1.pdf>. http://www.earthjournals.org/ijpt_issue1.html
7. Lydie N. Pani, Leslie Korenda, James B. Meigs, Cynthia Driver, Shadi Chamany, Caroline S. Fox, Lisa Sullivan, Ralph B. D. Agostino and David M. Nathan. "Effect of Aging on A1C Levels in Individuals without Diabetes: Evidence from the Framingham Offspring Study and the National Health and Nutrition Examination Survey 2001–2004", *Diabetes Care* October 2008 31:1991-1996. Doi: 10.2337/dc08-0577. <http://care.diabetesjournals.org/content/31/10/1991.full>
8. K. Wiener, N.B. Roberts, "Age does not influence levels of HbA1c in normal subject", *QJM: An International Journal of Medicine* Volume 92, Issue 3 Pp.169 - 173. DOI: <http://dx.doi.org/10.1093/qjmed/92.3.169>. <http://qjmed.oxfordjournals.org/content/92/3/169>
9. Sandrine Vallée Polneau, Virginie Lasserre, Michèle Fonfrède, Jacques Delattre, Simone Bénazeth, "A different approach to analyzing age-related HbA1c values in non-diabetic subjects", *Clinical Chemistry and Laboratory Medicine: CCLM / F E S C C* [2 0 0 4 , 4 2 (4) : 4 2 3 - 4 2 8] . DOI: 10.1515/CCLM.2004.074 (PMID: 15147153). <http://www.degruyter.com/view/j/cclm.2004.42.issue-4/cclm.2004.074/cclm.2004.074.xml>. <http://europepmc.org/abstract/MED/15147153>
10. Udaya M Kabadi, "Glycosylation of Proteins: Lack of Influence of Aging", *Diabetes Care* May 1988 vol. 11 no. 5 429-432 . doi: 10.2337/diacare.11.5.429 . <http://care.diabetesjournals.org/content/11/5.toc>
11. A. P. Yates and I Laing, "Age-related increase in haemoglobin A1c and fasting plasma glucose is accompanied by a decrease in β cell function without change in insulin sensitivity: evidence from a cross-sectional study of hospital personnel Article first published online: 26 MAR 2002", *Diabetic Medicine* Vol 19 Issue 3 DOI: 10.1046/j.1464-5491.2002.00644. <http://onlinelibrary.wiley.com/doi/10.1111/dme.2002.19.issue-3/issuetoc>. <http://onlinelibrary.wiley.com/doi/10.1046/j.1464-5491.2002.00644.x/abstract>. <http://www.ncbi.nlm.nih.gov/pubmed/11918628>
12. Frank Q. Nuttal, "Effect of age on the percentage of hemoglobin A1c and the percentage of total glycohemoglobin in non-diabetic persons Original", *Journal of Laboratory and Clinical Medicine*, Volume 134, Issue 5, November 1999, Pages 451–453 <http://www.sciencedirect.com/science/journal/00222143/134/5#> [http://www.translationalres.com/article/S0022-2143\(99\)90165-8/abstract](http://www.translationalres.com/article/S0022-2143(99)90165-8/abstract). DOI: [http://dx.doi.org/10.1016/S0022-2143\(99\)90165-8](http://dx.doi.org/10.1016/S0022-2143(99)90165-8)
13. Yoshiaki Hashimoto, Azusa Futamura, and Miharu Ikushima, "Effect of Aging on HbA1c in a Working Male Japanese Population", *Diabetes Care* October 1995 18:1337-1340 . doi:10.2337/diacare.18.10.1337 . <http://care.diabetesjournals.org/content/18/10/1337>
14. Rozing MP, Westendorp RGJ, De Craen AJM, Frölich M, De Goeij MCM, Heijmans BT, et al, "Favorable Glucose Tolerance and Lower Prevalence of Metabolic Syndrome in Offspring without Diabetes Mellitus of Nonagenarian Siblings: The Leiden Longevity Study", *Journal of the American Geriatrics Society* 2010 Volume 58, Issue 3 March 2010 Pages 564–569. <http://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2010.02725.x/full>
15. P. Ravi Kumar, A. Bhansali, R. Walia, G. Shanmugasundar and M. Ravikiran, "Alterations in HbA1c with advancing age in subjects with normal glucose tolerance: Chandigarh Urban Diabetes Study (CUDS)", *Diabetic Medicine* Volume 28, Issue 5, pages 590–594, May 2011. DOI: 10.1111/j.1464-5491.2011.03242.x <http://onlinelibrary.wiley.com/doi/10.1111/j.1464-5491.2011.03242.x/abstract>