IJMRP

International Journal of Medical Research Professionals

Original Article

High Glycated Hemoglobin Levels In Corelation With Ageing In Non-Diabetics

Gitanjali Goyal[1*], KMDS Panag[2], Sheenam[3], S.Jasmeet Singh[4]

[1*]Associate Professor, [2]Professor and Head, [3]MD Student, [4]Demonstrator, Department of Biochemistry, GGS Medical College, Faridkot, Punjab, INDIA.

Article History
Received: 15 Nov 2015
Revised: 19 Nov 2015
Accepted: 22 Nov 2015

***Correspondence to:**
Dr Gitanjali Goyal,
Associate Professor,
Deptt. Of Biochemistry,
GGS Medical College,
Faridkot.
gitanjaligoyal@yahoo.co.in

ABSTRACT

Introduction: Glycated Hemoglobin (HbA1c) is a measure of the degree to which hemoglobin is glycosylated in erythrocytes and is expressed as a percentage of total hemoglobin concentration. HbA1c has been regarded as an indicator of average glycemic values for patients with diabetes. Glycemia is recognized to change with age. According to American Diabetes Association guidelines, normal range for HbA1c levels is <6%. Present study aimed to find the effect of ageing on HbA1c, fasting and 2 hr post prandial glucose levels in non-diabetic subjects.

Material & Methods: The study included 100 non- diabetic subjects, aged 30-70 years, of both genders. These were further subdivided into 4 subgroups of age (i.e., 31- 40, 41-50, 51-60 and 61-70 years). Fasting blood sugar (FBS) and 2 hr post prandial glucose (PP) levels were estimated. HbA1c levels were estimated using boronate affinity assay.

Results: HbA1c levels rise with age, with the 97.5th upper limits for 40 years being 5.72 compared with 6.61or even higher for those aged upto70 years. The association was found to be extremely significant as all the p-values were <0.05.

Conclusion: In summary, our study found clearly that HbA1c increases with age with minimal increase in FBS and PP levels. The possibility for association of higher HbA1c with increase in age in non-diabetics is multifactorial including accumulation of toxic metabolic products, sedentary lifestyle, increased body and abdominal fat, impaired glucose metabolism, altered pulsatile insulin release and resistance to insulin. We recommend that further studies to be undertaken for the role of ageing as a confounding factor in estimating glycemic control with HbA1c.

KEYWORDS: Ageing, Glycated hemoglobin, Non- diabetics.

INTRODUCTION

Glycemia is recognized to change with age. The prevalence of diabetes and impaired glucose homeostasis is increased among older individuals.[1] Fasting plasma glucose (FPG) and the oral glucose tolerance test (OGTT) are considered to be appropriate tests for diagnosing pre-diabetes and/or diabetes while OGTT is also considered an appropriate test for assessing diabetes risk in patients with impaired fasting glucose (IFG).[2] As an alternative to these methods, an International Expert Committee, including representatives of the American Diabetes Association (ADA), the International Diabetes Federation (IDF), and the European Association for the Study of Diabetes (EASD), recently recommended evaluating glycosylated hemoglobin (HbA1c), with a cut-off point of ≥ 6.5% to diagnose diabetes[3] (the HbA1c of young, lean and healthy subjects is approximately 5.0%.[4] This strategy was endorsed and adopted by the ADA in 2010.[5] Glycated Hemoglobin A1c (HbA1c) is a measure of the degree to which hemoglobin is glycosylated in erythrocytes and is expressed as a percentage of total hemoglobin concentration.

Epidemiological evidence suggests that elevated HbA1c is associated with cardiovascular and ischemic heart disease risk.[6] Both obesity and physical inactivity are considered to play important roles in the prevention and treatment of diabetes, with the ADA recommending that people with HbA1c of 5.7-6.4% undergo moderate weight loss (7% of initial body mass), as well as increasing physical activity to at least 150 min/week of moderate activity.[7]

Ageing is another factor that contributes to variance in HbA1c and diabetes risk. Even in non-diabetic adults with normal fasting glucose, HbA1c steadily increase with age, such that at 70+ years of age it is 5.5%, almost

attaining the ADA criterion for prediabetes.[5] It should be noted, however, that ageing is also associated with a number of risk factors common to the sedentary/obese lifestyle that are expected to be associated with elevated HbA1c levels, including increased body and abdominal fat,[8,9] a more atherogenic lipid profile,[10,11] diabetes[12], elevated inflammatory markers[13], decreased cardiorespiratory fitness[14] and reduced physical activity.[15,16] Any, or all, of these risk factors are expected to be associated with elevated HbA1c levels. There is, however, little information as to what extent factors such as obesity or physical inactivity in older adults modify HbA1c levels above and beyond the effect of aging, *per se*. This knowledge is essential for determining whether or not 1) lowering HbA1c by diet and exercise is a realistic goal for obese and inactive elderly subjects and 2), if this is indeed achievable, what should be the target levels HbA1c to attain?

Current HbA1c targets for diabetes treatment set by the ADA (<7%) or The American College of Endocrinology (<-6.5%) are not age specific. The central role played by HbA1c in management of diabetes and possibly in its diagnosis raise the question whether there are age related differences in HbA1c.[5,17] Even in non-diabetic adults with normal fasting glucose, HbA1c steadily increases with age and at about 70 years of age, it is 6.61%, almost attaining the ADA criterion for pre diabetes. According to ADA guidelines, normal range for HbA1c levels in non- diabetics is <6%. Abnormal carbohydrate metabolism is also observed in obese especially with a central distribution of body fat, along with decrease in physical activity which occur progressively with ageing.[18] The present study was aimed to find the levels of HbA1c in persons of different age groups.

MATERIALS AND METHODS

The study included 100 non- diabetic patients, aged 30-70 years, of both genders visiting GGS Medical College and Hospital, Faridkot, Punjab. Informed consent was taken before enrolling the patients.

Patients were divided into 4 subgroups by age (i.e. 31-40, 41-50, 51-60 and 61-70 years). Fasting blood sugar (FBS) and 2 hr post prandial glucose (PP) levels were estimated. Oral GTT was done to exclude impaired glucose tolerance. HbA1c levels were estimated using boronate affinity assay.

Subjects with impaired FPG, IGT by OGTT and/or diabetics were excluded from the study. Similarly subjects on medications which can alter the concerned parameters were excluded from the study. Statistical analysis was done using SPSS.

RESULTS

This study showed that HbA1c levels rise with age, with the 97.5th upper limits for 40 years being 5.72 compared with 6.61or even higher for those aged upto70 years. Association found was extremely significant as all the p-values were <0.05.

To determine whether FBS and PP contribute to the increase in HbA1c observed with age, we analyzed FBS and PP by age categories which showed marginal increase but the values were in normal range as per ADA guidelines for non- diabetics.

In summary, our study found clearly that HbA1c increases with age as shown in Table-2 and depicted in Figure-2 with marginal increase in FBS and PP levels as shown in Table-1 and presented in Figure-1. There was a significant positive association between mean HbA1c and age- groups in the non-diabetic persons.

Table1- Fasting and 2-hr PP glucose values in non-diabetics with different age groups

Age groups (years)	n (no. of patients)	Fasting blood sugar (FBS)mg/dl	Post-prandial sugar (PP)mg/dl
31-40	12	91.81	93.16
41-50	33	93.20	98.62
51-60	39	96.42	107.53
61-70	16	99.01	125.41

Table 2— Mean and 97.5th percentile HbA1c among non-diabetics of different age groups

Age groups (years)	n (no. of patients)	HbA1c (%) (Mean ± SE)	HbA1c (%) (97.5th percentile)
31-40	12	5.20 ± 0.01	5.72
41-50	33	5.20 ± 0.02	6.26
51-60	39	5.28 ± 0.03	6.51
61-70	16	5.50 ± 0.04	6.61

DISCUSSION

The process of ageing and death remain one of the most fascinating and mysterious areas of biological research. With increased longevity, the projected population above 65 or older will be one fifth of world population.[19] One of the hypothesis trying to explain the process of ageing is the idea of glycation of proteins.[20] Ageing process can be faster because of accumulation of toxic metabolic products. These substances could be products of non-enzymatic glycosylation. Glycosylation may therefore play an important role in ageing and has been implicated in the pathophysiology of number of diseases, like Alzheimer disease, diabetes, and lung diseases.[21] One such explanation may be changes in the rate of glycation associated with ageing. Ageing is also associated with many risk factors common to the sedentary lifestyle that are expected to be associated with elevated HbA1c levels, including increased body and abdominal fat, a more atherogenic lipid profile, diabetes, elevated inflammatory markers, decreased cardiorespiratory fitness and reduced physical activity. A possible

explanation for the observed association of higher HbA1c with increasing age in individuals with normal glucose tolerance is that factors unrelated to glucose metabolism are affecting HbA1c levels. Similar results were observed in a twin community based population study, strengthening our conclusion that HbA1c levels increase with age.[4] Moreover, this also enhances the generalizability of our results. The possible explanation for this association of higher HbA1c with increasing age in non-diabetics is that factors unrelated to glucose metabolism are affecting HbA1c levels.

Considering the value of HbA1c in the elderly, glycation may play independent role in ageing.[20] The results of a large cross sectional study shown the body wt and BMI increase throughout life till 50-60 years of age and obesity especially with a central distribution of fat along with reduction in physical activity occur progressively with ageing and both these adversely affect carbohydrate metabolism.[18] Another study demonstrated positive correlation between the age group over 60 years with HbA1c.[20]

Figure 1: Fasting and 2-hr PP glucose values in non-diabetics with different age groups

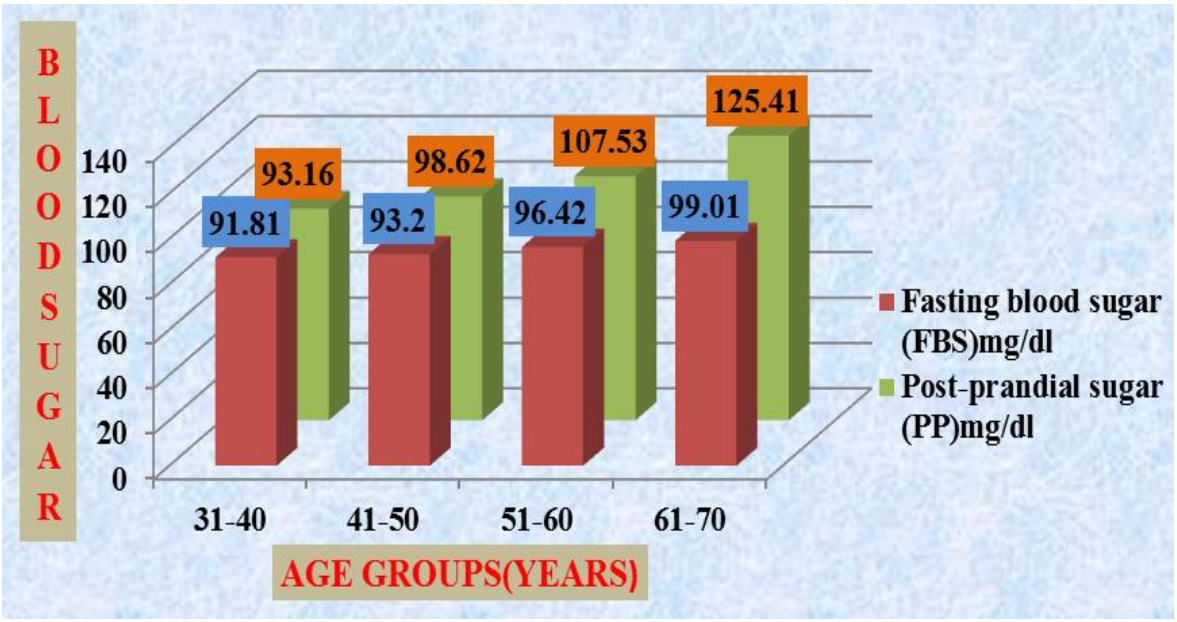
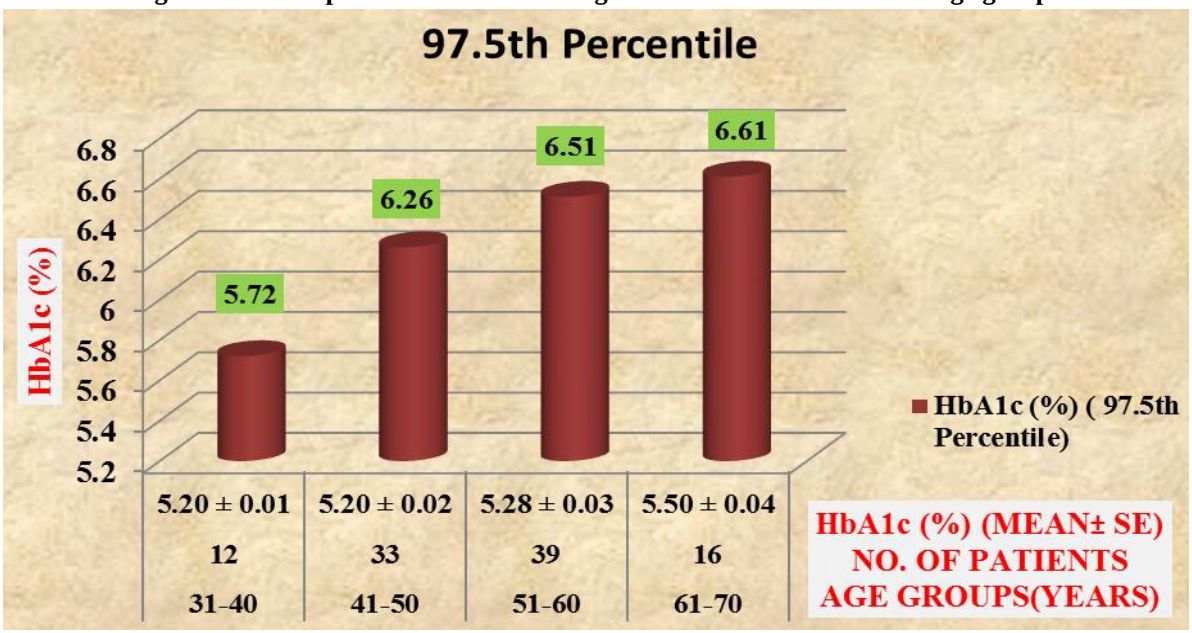


Figure 2 : 97.5th percentile HbA1c among non-diabetics with different age groups



Pathogenic mechanisms which contribute to glucose intolerance with ageing include alteration in glucose induced insulin release, resistance to insulin mediated glucose disposal.[22] This may be partly due to decreased beta cell response to the hormones and altered pulsatile release of insulin.[23]

Our findings were in discordance with some studies which say that there is no relation between age and HbA1c.[24]

Age has been associated with deterioration in cardiorespiratory fitness.[14] Time spent in sedentary activities has also been reported as increasing with

age.[25,26] which is a predictor of obesity, atherosclerosis, and cardiovascular disease.[27,28] Some studies have found that weakening of the cardiovascular system associated with ageing could be countered by increasing levels of physical activity and functional fitness.[17,29,30] Poor Glycemic control (HbA1c ≥ 8%) has been found to explain approximately 10% of disability, i.e. difficulty to perform a physical task by participants aged ≥ 60 years which increases to 85% if we include comorbidities, mostly cardiovascular disease and obesity.[16] Additionally, it remains to be understand the effect of sex on the relationship between functional fitness and HbA1c in elderly.

Gao and colleagues, studying a population with mean HbA1c of 5.8% and 91% of HbA1c values below 7%, have partially agreed concluding that HbA1c was not associated with risk of developing instrumental activities of daily living (IADL) and/or activities of daily living (ADL) impairment in the whole sample population, however it was associated when analyzing only women.[6]

CONCLUSION

In nutshell, the study done by our department clearly indicated that HbA1c increases with age and analysis of FBS and PP by age categories showed marginal increase but the values were in normal range as per ADA guidelines for non-diabetics. Association found was extremely significant as all the p-values were <0.05. We, therefore recommend that ageing may be undertaken as a confounding factor in estimating glycemic control using HbA1c levels.

REFERENCES

1.Davidson MB. The effect of ageing on carbohydrate metabolism: a review of the English Literature and a practical approach to the diagnosis of diabetes mellitus in the elderly. Metabolism 1979; 28:688-705

2.American Diabetes Association: Standards of medical care in diabetes- 2009. Diabetes Care 2009, 32:S13-S61.

3. International Expert Committee: International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009, 32:1327-34.

4. Pani LN, Korenda L, Meigs JB, Driver C, Chamany S, Fox CS et al. Effect of aging on A1C levels in individuals without diabetes. Diabetes Care 2008; 31:1991-6

5. American Diabetes Association: Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2010; 33:S62-9.

6. Gao L, Matthews FE, Sargeant LA, Brayne C, MRC CFAS. An investigation of the population impact of variation in HbA1c levels in older people in England and Wales: from a population based multi-centre longitudinal study. BMC Pub Health 2008; 8:54.

7. American Diabetes Association: Standards of medical care in diabetes- Diabetes Care 2011; 34:S11-S61.

8. Kohrt WM, Obert KA, Holloszy JO. Exercise training improves fat distribution patterns in 60 to 70-year old men and women. J Gerontol 1992; 47:99-105.

9. Ryan AS, Nicklas BJ. Age-related changes in fat deposition in midthigh muscle in women: relationships with metabolic cardiovascular disease risk factors. Int J Obes Relat Metab Disord 1999; 23:126-32.

10. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998; 21:518-24.

11. Short KR, Vittone JL, Bigelow ML, Proctor DN, Rizza RA, Coenen-Schimke JM et al. Impact of aerobic training on age-related changes in insulin sensitivity and muscle oxidative capacity. Diabetes 2003; 52: 1888-96.

12. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes : estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.

13. Pedersen M, Bruunsgaard H, Weis N, Hendel HW, Andreassen BU, Eldrup E et al. Circulating levels of TNF alpha and IL-6-relation to truncal fat mass and muscle mass in healthy elderly individuals and in patients with type-2 diabetes. Mech Ageing Dev 2003; 124:495-502.

14. Fleg JL, Morrell CH, Bos AG, Brant LJ, Talbot LA, Wright JG et al. Accelerated longitudinal decline of aerobic capacity in healthy older adults. Circulation 2005; 112:674-82.

15. Gregg EW, Beckles GL, Williamson DF, Leveille SG, Langlois JA, Engelgau MM et al. Diabetes and physical disability among older U.S. adults. Diabetes Care 2000; 23:1272-77.

16. Kalyani RR, Saudek CD, Brancati FL, Selvin E. Association of diabetes, comorbidities, and A1C with functional disability in older adults: results from the National Health and Nutrition Examination Survey (NHANES)1999-2006. Diabetes Care 2010; 33:1055-60.

17. Martins RA, Veríssimo MT, Coelho Silva MJ, Cumming SP, Teixeira AM. Effects of aerobic and strength-based training on metabolic health indicators in older adults. Lipids Health Dis 2010; 9:76.

18. Meneilly G.S, Tessier D. Diabetes in elderly adults. J Gerontol 2001;56A 5.

19.Krikwood T. Time of our lives: the science of human ageing by Tom Kirkwood. Oxford University press. 2001;ISBN:0195139267.

20.Dziedzic M, Halabis M, Kuna J, Lenart –Lipinsika M and Solski J. The level of glycated haemoglobin (HbAic) in healthy subjects. Annales Universitatis Mariae Curie-Sklodowska 2010;23N2,16

21.Trypuc AJ, Czerpak R. The role on non enzymatic glycosylation of proteins in ageing processes and

pathogenensis of geriatric diseases. Post Biol Kom 2007;34:683.
22.Muller DC, Elahi D, Tobin JD, Andres R. The effect of age on insulin resistance and secretion: a review. Semin Nephrol 1996;16:289.
23.Meneilly GS, Velduis JD, Elahi D. Deconvolution analysis of rapid insulin pulses before and after six weeks of continous subcontinous administration of GLP-1 in elderly patients with type 2 diabetes. J Clin Endo Meta 2005; 6251:90.
24.Winer K, Roberts NB. Age does not influence level of HbA1c in normal subjects. Q J Med 1999;169:92.
25. Schoenborn CA, Adams PF, Barnes PM, Vickerie JL, Schiller JS. Health behaviors of adults: United States, 1999-2001. Vial Health Stat 2004;219:1-79.
26. Thune I, Njolstad I, Lochen ML, Forde OH. Physical activity improves the metabolic risk profiles in men and women. Arch Intern Med 1998;158:1633-40.
27. Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med 2002; 162:1867-72.
28. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341: 1097-1105.
29. Black MA, Green DJ, Cable NT. Exercise prevents age-related decline in nitric-oxide-mediated vasodilator function in cutaneous microvessels. J Physiol 2008; 586:3511-24.
30 Trott DW, Gunduz F, Laughlin MH, Woodman CR. Exercise training reverses age-related decrements in endothelium-dependent dilation in skeletal muscle feed arteries. J Appl Physiol 2009; 106:1925-34.

How to cite the article: Gitanjali Goyal, KMDS Panag, Sheenam, S.Jasmeet Singh. High Glycated Hemoglobin Levels In Corelation With Ageing In Non-Diabetics. Int J Med Res Prof. 2015, 1(3); 35-39.