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Glycated haemoglobin levels in non-diabetics: The effect of ageing

Bhumija Sharma* Pallavi Mahajan** Suvarna Prasad*** Rajesh Pandey**** Jasbir Singh***** K.S.Sodhi***

*BAMS, MSc(Medical Bio chemistry final year PG student)
** MBBS, MD(second year PG student in Biochemistry)
*** MD, Professor of Biochemistry
**** MD, Associate Professor of Biochemistry
*****MD, Professor and HOD of Biochemistry
Maharishi Markandeshwar Institute Of Medical Science and Research, MULLANA [MMIMSR]

Corresponding author: Dr. Bhumija Sharma Msc. medical biochemistry
Maharishi Markendeshwar Institute of Medical Science and Research [MMIMSR], Mullana, Ambala 133004 Haryana India. Email: bhumijasharma@yahoo.co.in

ABSTRACT

Aim: To find out the correlation if any, between glycosylated haemoglobin (HbA1c) levels and age of non-diabetic people.

Material and methods: This study included 246 non-diabetic subjects who were grouped according to age and gender. Their HbA1c levels were estimated by ion- resin method. Average blood glucose was also calculated.

Results: Results came out to be as expected. There was significant association between age and HbA1c levels. Mean age and HbA1c in males was (45.76, 5.26), in females (46.72, 6.18) respectively. Correlation coefficient came out to be highly significant with r=0.207and p value=0.00049. Mean HbA1c for different age groups {20-39,40-59,60-79years } were as follows –{5.38,5.88,5.92} respectively.

Conclusion: Glycosylated Hb varies with age and this should be considered, whenever HbA1c levels are to be measured to assess the level of glycemic control especially in elderly diabetic people.

Keywords: Glycosylated, age, gender, hemoglobin

INTRODUCTION

Since 1968, glycosylated hemoglobin (HbA1c) has been regarded as an indicator of average glycemic values for patients with diabetes [1]. However, it was not until 1977 that its potential as an indicator of glycemic control was first recognized. During the last 30 years, HbA1c has played a vital role in the monitoring of diabetes with a firm evidence base from the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) [2]. Glycosylated hemoglobin (GHb) is formed continuously by the adduction of glucose by covalent bonding to the amino-terminal valine of the hemoglobin beta chain progressively and irreversibly over a period of time. This glycation process may alter the structure and function of proteins and thus be relevant to the small-vessel complications of patients with diabetes mellitus, glycation of haemoglobin and serum proteins (in the form of fructosamine) has become an important means of objectively assessing glycaemic control in diabetic patients[3] . HbA1c is stable till the life of the red blood cell and glucose is released upon the dissolution of the red blood cell. The half life of the red blood cell is 60 days. Therefore, the HbA1c test could indicate the average glycemic level during the past 2-3 months [4]. Furthermore GHb is unaffected by diet, insulin, drugs, or exercise on the day of testing. But there have been some reports about the relationship between age and HbA1c level [3]. While the role of HbA1c in monitoring diabetes has intensified, that of glucose has diminished. Thus, the present study was aimed to find the effect of aging on the HbA1c levels in normo glycemic individuals.

MATERIALS AND METHODS

The study population consisted of 246 non-diabetic subjects, aged 20-79 years, of both genders visiting o.p.d and hospital laboratory of Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. Samples of the venous blood were collected in EDTA vials. HbA1c levels were estimated using Ion Exchange Resin method [5]. All the diabetic patients were excluded from this study. These 246 subjects were further subdivided into 2 subgroups according to their gender and 3 subgroups of age. Their mean blood glucose

was estimated by the following formula - [eAG mg/dl=28.7×HbA1c − 46.7] , where eAG -estimated average glucose [6]

RESULTS

We categorized age into 3 groups of (i.e, 20-39, 40-59 and 60-79 years).HbA1c levels were analysed according to age and sex. Among 246 subjects, 143 were male (58.13%) and 103 females (41.8%). In table no1. mean age of males was 45.76 with standard deviation (SD) of 14.59, standard error mean (SEM) 1.22. Mean age of females was 46.2 with SD of 13.47 and SEM 1.33. Independent t-test was done to find out the association among age and sex and insignificant p- value was found (t= 0.525, p=0.599), as it was more than 0.05. HbA1c mean calculated for males was 5.26 ±1.14 with SEM of 0.09, for females mean HbA1c was 6.18±1.67, SEM 0.16, (t =5.078, p =0.0001), as p-value is (<< 0.05), it is extremely statistically significant. Therefore association of HbA1c levels with age was significant in both sexes. Pearson´s correlation of age with HbA1c levels in both the genders was highly significant where p<<0.05 [r=0.156 for males, r=0.240 for females].Table no 2 includes descriptive statistics of HbA1c according to different age groups in both sexes. Significant association was found between HbA1c levels and different age groups. In males, mean HbA1c ranges from (5-5.37) and in females, range is (5.76-6.47). Association found was extremely significant as all the p-values were <<0.05. In Table 3, mean blood glucose was calculated by above given formula and its relation with age was found. In table 4 descriptive statistics of age and average blood glucose among both genders is given, again with all p-values to be extremely significant. HbA1c levels are depicted in figure1 according to age and gender. Scatter plot of HbA1c and age is shown in figure2.

DISCUSSION

We examined whether HbA1C increases with age: by examining 246 different non-diabetic subjects with no evident abnormalities of glucose metabolism. We observed that HbA1C levels are increasing with age and was found to be more in females. The age-related increase in HbA1c observed in our study is similar to that in previous studies: one in Japan [7] and one in a very small (*n* - 109) convenience cohort in the U.S [8]. 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 [9]. 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 disease, like Alzheimer disease, diabetes, and lung diseases [10].One such explanation may be changes in the rate of glycation associated with aging [3,11]. There is no evidence for decreased red cell turnover owing to decreased clearance with aging as a possible explanation. It is possible that other factors such as worsening kidney function with aging or anaemia could be playing a role; however, these are less likely to play a significant role in healthy aging adults.

It is important to determine whether the change in glucose tolerance with aging is attributable to the aging process itself or to other age-related factors, such as concomitant disease, medication, BMI, the change in distribution of body fat and reduction in physical activity. Subjects included were apparently healthy without acute or serious chronic illnesses. The elevation of HbAlc with age was not influenced by the level of physical activity [7].

Some reports have demonstrated an association of HbA1c with age while others have not. Arnetz et al [12] observed differences in HbA1c levels between the age groups, with oldest having highest values, same like us. Nuttal et al. reported that hba1c level increased with age[8]. Marcin et al. found that elevated HbA1c levels increased with levels of glucose as an effect of ageing [13].Chi-chang liang1 et.al, stated that among the general population, the HbA1c value increases with age, but gender does not significantly impact the HbA1c value. On the contrary, Winer [14] and E.S Kilpatrick [3] were unable to detect any direct relationship between age and HbA1C.

There are several limitations of this study. First, the number of subjects is small. Secondly, females were less in number. Thirdly, we did not compared fasting and post prandial levels of glucose. We had not done this comparison on young children. Finally, we did not account for the prevalence of other conditions that could affect HbA1C levels, kidney dysfunction or anaemia.

CONCLUSION

In this study, the uniform results clearly establish that HbA1C increases with age.

Except in some controversial papers with small sample size that show a lack of influence of age on glycohemoglobin, most data have demonstrated an elevation of glycohemoglobin with age We recommend that further studies be undertaken to determine whether the increase in HbA1C associated with age in subjects with normal glucose tolerance is significant for practioners and to discover whether its diagnostic and treatment criteria would be appropriate. To our knowledge, this is not the largest study to evaluate the relationship between HbAlc and aging. Results are suggesting that aging itself may cause an increase in HbAlc independently, further more investigation in this area is mandatory.

Table1.Descriptive statistics of the 246 Patients according to their Sex.

	Sex	N	Mean	Std. Deviation	Std. Error Mean	**T value**	**P value**
Age in years	Male	143	45.76	14.59	1.22	0.525	0.599
	Female	103	46.72	13.47	1.33		
HbA1c Levels	Male	143	5.26	1.14	0.09	5.078	0.0001*
	Female	103	6.18	1.67	0.16		

Pearson correlation	r=0.207	1sided	0.000493	
		2sided	0.000987	
	male	r=0.156	1sided	0.0309
			2sided	0.06191
	female	r=0.240	1sided	0.00734
			2sided	0.01468

Independent t test have been between means , *p value < 0.05 have been considered to be significant

Table 2 : Descriptive Statistics of the HbA1c

	Age Groups	Sex	N	Mean	Std. Deviation	Std. Error	T value	p value
HbA1c Levels	20-39	Male	48	5.00	1.01	0.15	2.34	0.022*
		Female	32	5.76	1.88	0.33		
	40-59	Male	58	5.44	1.21	0.16	3.31	0.001*
		Female	47	6.32	1.51	0.22		
	60-79	Male	37	5.37	1.19	0.20	3.05	0.003*
		Female	24	6.47	1.63	0.33		
	Independent t test have been between means , *p value < 0.05 have been considered to be significant							

Table 3. Statistics for average blood glucose

Age groups	N	Average Blood glucose(mg/dl)	SD	SEM	T value	P value
20-39	80	105.61	41.90	4.68	2.46	0.0148
40-59	105	120.65	40.62	3.96		
					1.98	0.0488
60-79	61	119.80	42.11	5.39		

a) Independent t test have been between mean blood glucose levels , *p value < 0.05 have been considered to be significant

Table 4. Descriptive statistics for average blood glucose for 246 subjects							
Age group	**Gender**	**N**	**Avg blood glucose**	**SD**	**SEM**	**T value**	**P value**
20-39	males	48	96.93	28.94	4.17	2.33	0.022
	females	32	118.64	53.97	9.5		
40-59	males	58	109.35	34.75	4.56	3.317	0.0013
	females	47	134.61	43.30	6.31		
60-79	males	37	107.4	34.07	5.6	3.048	0.0034
	females	24	138.9	46.686	9.5		

a) Independent t test have been between means , *p value < 0.05 have been considered to be significant

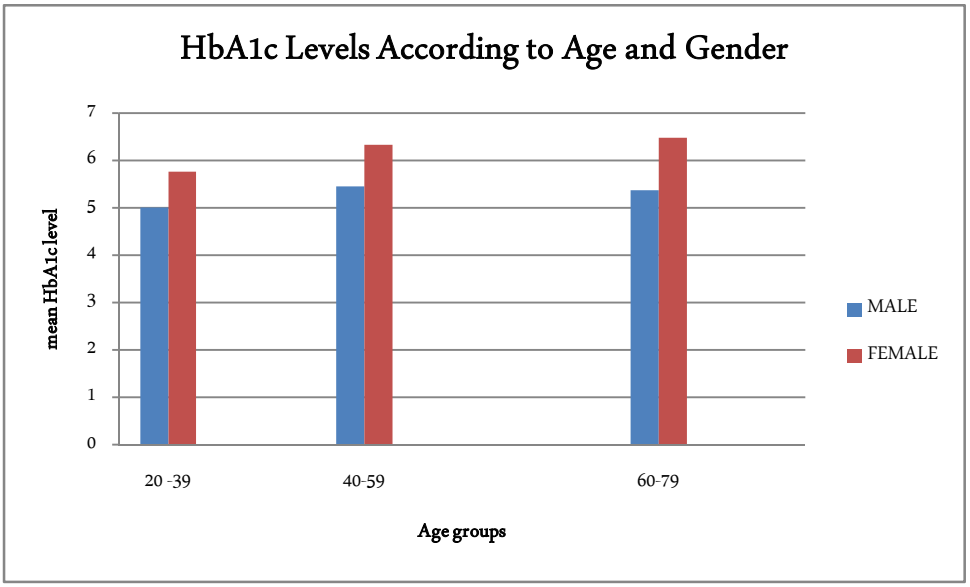

FIGURE: 1

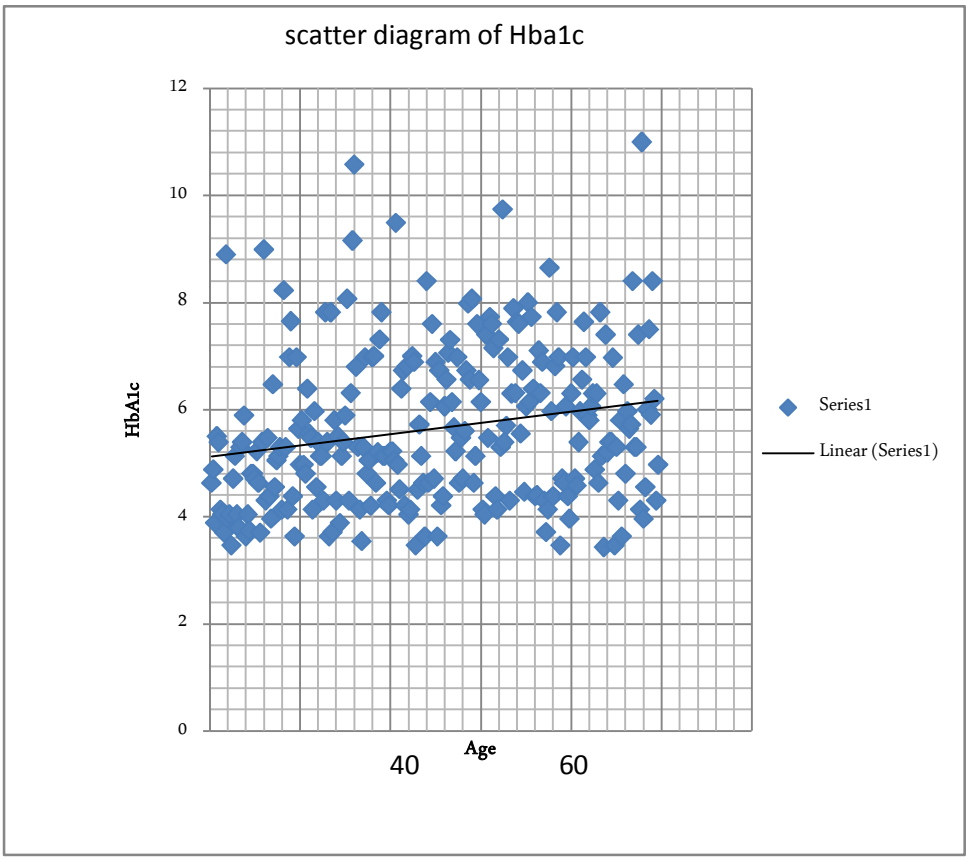

FIGURE: 2

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