ISSN: 2278-778X
Research Article
www.ijbio.com

EVALUATION OF GLYCATED ALBUMIN AND DYSLIPIDEMIA IN TYPE-2 *DIABETES MELLITUS*

Suresh Babu Kondaveeti[1], Ivvala Anand Shaker[1], Aravind Kumar R[2], Hemraz palwan[3], Raja G[1]
[1]Department of Biochemistry, Melmaruvathur Adhiparasakthi Institute of Medical Science & Research, Melmaruvathur, Tamil Nadu, India
[2]Department of Physiology, Melmaruvathur Adhiparasakthi Institute of Medical Science & Research, Melmaruvathur, Tamil Nadu, India
[3]Ottawa Fertility Centre, 66 – 890 Cahill Dr (W), Ottawa, ON K1V 9A4, Ottawa, Canada

Corresponding Author: Mr. Suresh Babu Kondaveeti, Department of Biochemistry, Melmaruvathur Adhiparasakthi Institute of Medical Science & Research, Melmaruvathur, Tamil Nadu, India

Received for publication: July 13, 2012; **Accepted**: September 24, 2012.

Abstract: Diabetic patients with accompanied (but often unnoticed) dyslipidemia are soft targets of cardiovascular deaths. An early intervention to normalize circulating lipids shown to reduce cardiovascular complications and mortality. Now a day's Glycated albumin (GA) is a routinely used marker for short-term glycemic control. This investigation is an attempt to evaluate the association between GA and various lipid parameters. Venous blood samples collected from 100 type-2 diabetic patients (46 males, 44 females) and serum analyzed for GA, Fasting blood glucose, Total Cholesterol, Triacylglycerols, HDL-C and LDL-C. L/H risk ratio is also calculated. The levels of GA (%) did not differ significantly between males (8.51 ± 1.17) and females (8.24 ± 1.89), whereas male patients had higher mean values of FBG and various lipid parameters than in females. Patients with GA value >17.0 % showed direct and significant correlation with FBG, TC, LDL-C, L/H risk ratio as compared to patients with GA ≤ 17.0%. There was no significant difference in TG, HDL-C between two groups of glycated albumin. These findings indicate that GA is utilized for screening high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs.

Keywords: Diabetes, Dyslipidemia, Glycated Albumin.

INTRODUCTION

Diabetes Mellitus has become a major health problem in India. It has been estimated that the burden of Type-2DM for 2DM are considerable: as a lifelong disease, it increases morbidity and mortality and decreases the quality of life. At the same time, the disease and its complications cause a heavy economic burden for diabetic patients themselves, their families and society [1] [2]. Diabetes is a global endemic with rapidly increasing prevalence in both developing and developed countries [3]. The International Diabetes Federation (IDF) reported that total number of diabetic subjects in India is 41 million in 2006 and that this would raise to 70 million by the year 2025 [4]. Studies on migrant Indians have shown that they have a higher predisposition to insulin resistance, type-2 diabetes and coronary artery disease compared to other ethnic groups [5]. There is a higher risk of cardiovascular disease in people with type-2 diabetes, while cardiovascular deaths represent the top killer in this population [6]. Epidemiological studies have demonstrated that diabetes mellitus is an independent risk factor for cardiovascular disease and it amplifies the effects of other common risk factors such as smoking, hypertension and dyslipidemia [7]. Hyperlipidemia is one of the most risk factors for coronary artery disease (CAD) which is more prevalent among adults with type-2 diabetes mellitus than in the general population with a four to six fold greater cardiovascular mortality [8].

The concept of estimating glycated albumin (GA) is proving to be an important tool in assessing short term glycaemic control of diabetic patients. Previously adequate studies have been done to prove the efficacy of HbA1c, but considering its limitations, certain other tests like glycated proteins is being looked at to overcome such circumstances. Glycated Haemoglobin (HbA1c) which is an index of long term glycaemic control (2-3 months) in diabetic patients is measured in majority of patients worldwide[9][10]. Since glycation takes place throughout the life span of hemoglobin and serum proteins. glycated albumin has been thought to reflect short term variations of glycaemic control. Levels of glycated protein reflect the degree of hyperglycemia during their life span. The turnover of serum albumin is more rapid (15-20 days) than haemoglobin, it has become clear that glycated albumin plays a dual role: as an indicator or marker of intermediate glycation, and as a causative agent of the damage of diabetes complications. By products of albumin glycation have been specifically implicated as causal factors in atherosclerosis (including coronary

artery disease) and kidney failure, two of the most extensive and most serious complications of diabetes. Hence glycated albumin is useful for the evaluation of short term glycemic control (2-4 weeks) in patients with diabetes [11][12][13][14]. Positive relationship between glycated albumin (GA) and cardiovascular disease shown in non diabetic cases even within normal range of GA. This study was conducted to know the relationship between glycemic control and serum lipid profile and evaluated the importance of glycated albumin (GA) as an indicator of dyslipidemia in type-2 diabetic patients.

MATERIALS AND METHODS

The study comprised of a total of hundred Type-2 diabetic patients (26 males and 24 females) The study group comprised of type-2 diabetic patients at two tertiary health centers located at Kanchipuram, Tamil Nadu, The present study was conducted from January 2009 to December 2011 in The study included subjects with a known history of Type-2DM and age above 40years [based on the screening recommendation by American Diabetes Association (ADA). Ethical clearance obtained for the study from the hospital. Venous blood samples collected from all the patients after at least 10 hours fasting into centrifuge tubes. The blood allowed to clot and then centrifuged at 3000 rpm for 15 min at room temperature. Plasma glycated albumin (GA) levels were measured by an enzymatic method using albumin specific protease, ketoamine oxidase and albumin assay reagent on the Hitachi autoanalyser 912 (Lucica GA-L, Asahi Kasei Pharma Corp, Tokyo, Japan) [15][16]. GA was hydrolyzed to amino acids by albumin specific proteinase and then oxidized by ketoamine oxidase to produce hydrogen peroxide, which was measured quantitatively. The GA value was calculated as the percentage of GA relative to total albumin, which was measured with bromocresol purple method. The measured value of GA was not influenced by the substances such as bilirubin F up to 14.6mg/dl, bilirubin C up to 15.2 mg/dl, glucose up to 1000 mg/dl, and ascorbic acid up to 100 mg/dl. The serum analyzed for total cholesterol by enzymatic (CHOD-PAP) colorimetric method and triglycerides by enzymatic (GPO-PAP) method [17]. HDL-Cholesterol estimated by precipitant method [18] and LDL-Cholesterol by Friedewald formula [18] as shown below.

LDL-C = TC - HDL-C – (TG/5)

The serum glucose determined by using the glucose oxidase enzymatic method [18]. All the parameters under investigation were determined in the serum of the subjects using commercially available reagent kits. For serum lipid reference level National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline was referred. According to NCEP ATP III guideline hypercholesterolemia defined as TC > 200mg/dl, high LDL-C when value > 100mg/dl, hypertriglyceridemia > 150mg/dl and low HDL-C when value < 40mg/dl. Dyslipidemia defined by presence of one or more than one abnormal serum lipid concentration. Values of GA were given as % of total albumin and values of all other parameters were given in mg/dl. All values were expressed as mean ± SD. Independent samples t test (2 tailed) was used to compare means of different parameters. Pearson's correlation test performed to examine various correlations.

RESULTS

Hundred Type-2 diabetic subjects included in the study out of which 46 were males and 44 were females. The mean age ± SD of male and female subjects were 56.36 ± 9.28 and 54.48 ± 14.06 years respectively. The mean value of GA and FBG were higher in males in comparison to female subjects but the differences were non-significant. Among circulating lipids the mean values of total cholesterol, triacylglycerols, LDL-C, HDL-C were higher in males than female patients. These differences were statistically non Significant

Table. 1: Lipid Profile Parameters between Male and Female Type-2 Diabetic Patients

Parameters	Males (n=46) Mean ± SD	Females (n=44) Mean ± SD	t-table value
Fasting Blood Glucose	168.50 ± 69.42	156.00 ± 66.25	0.65
Total Cholesterol	186.19 ± 52.28	173.46 ± 41.74	0.95
Triacylglycerols	174.38 ± 112.14	143.50 ± 56.51	1.22
HDL-C	39.35 ± 8.53	38.42 ± 7.46	0.41
LDL-C	111.97 ± 85.20	106.34 ± 75.38	0.57
Glycated albumin (GA)	8.52 ± 1.18	8.25 ± 1.90	0.61

Legend HDL-C = high density lipoprotein – cholesterol, LDL-C = low densitylipoprotein – cholesterol

Hypercholesterolemia was found in 46 (52%) subjects, similarly hypertriglyceridemia was found in 44 (48%), decreased HDL-C was found in66 (66%) and increased LDL-C was found in 60 (60%) subjects. seventy two(72%) subjects had only one abnormal lipid profile parameter, 56 (56%) had two abnormal lipid parameter, 22 (22%) had more than two abnormal lipid profile parameter. According to NCEP ATP III guidelines, 30 (58%) males out of 46 and 32 (67%) females out of 44 were dyslipidemic. Highly significant correlation observed between FBG and glycated albumin (GA) (r=0.338). glycated albumin (GA) also demonstrated direct and significant correlation with TC (r=0.309), LDL-C (r=0.306). The correlation between glycated albumin (GA) with TG (r=0.189) and HDL-C (r=0.104) was slightly positive, and it was statistically non significant.

Table.2 shows classification of subjects into two groups as per their glycemic index. First group consists of patients with GA value ≤ 17.0% and second group with GA value > 17.0%. The mean values of TC, TG, LDL-

C, LDLC/ HDL-C and L/H risk ratio were high in patients with GA >1 7.0%. FBG was significantly higher in second group when compared to first group.

Table. 2:

Parameters	Glycated albumin(GA)		t-table value
	< 17.0 % (n=40) Mean ± SD	> 17.0 % (n=60) Mean ±SD	
TotalCholesterol (TC)	174.30 ± 49.15	183.93 ± 46.72	0.80
Triacylglycerols	147.20 ± 70.03	167.80± 102.03	0.82
HDL-C	38.30 ± 9.52	39.30 ± 6.86	0.59
LDL-C	29.44 ± 14.01	33.56 ± 20.41	0.81
Risk ratio (TC / HDL-C	0.77 ± 0.30	0.86 ± 0.52	0.68
LDL-C / HDL-C	2.83 ± 1.89	2.88 ± 2.08	0.20
Fasting Blood Glucose	133.75 ± 43.17	181.67 ± 74.78	2.78**

DISCUSSION

In the present study, the pattern of lipid profile parameters in diabetic subjects and its correlations with glycated albumin (GA) are seen. The levels of glycated albumin (GA) and FBG did not differ significantly between male and female subjects. The mean values of TC, TG, HDL-C, LDL-C were higher in males as compared to female type-2 diabetic patients. However, Wexler [19] reported that mean values of TC and LDL-C were significantly higher in females as compared to males. This study reveals high prevalence of dyslipidemia is a well known risk factor for cardiovascular diseases. Insulin affects the liver apolipoprotein production which regulates the enzymatic activity of lipoprotein lipase (LpL) and cholesterol ester transport protein which are the factors leading to dylipidemia in Diabetes mellitus [20]. Insulin deficiency reduces the activity of hepatic lipase and several steps to produce altered LpL in diabetes mellitus [21]. A highly significant correlation between glycated albumin (GA) and FBG in this study is similar with previous studies [22][23]. Significant correlation between GA and TC, LDL-C also observed. In various studies glycated albumin (GA) was found to have positive correlation with TC, LDL-C and TG in diabetic patients [24][25]. In the present study the association between GA with various Lipid parameters and LDL-C-HDL-C ratio, suggests the importance of glycemic control in order to control dyslipidemia. The normal cut off value for glycated albumin (GA) in our population was derived using control group and it was 15% (range 7-17%) was said to be appropriate for reducing the risk for cardiovascular complications [26]. In the present study, diabetic patients were divided into two groups as per the cutoff of 7.0-17 %. The diabetic patients with GA value < 17.0 % showed increased mean values of TC, TG, LDL / HDL-C ratio and risk ratio; but it was statistically non significant in comparison to patients with glycated albumin (GA) value 7.0-17 % reported the impact of glycemic control on various lipid parameters and observed the significant alterations in all lipid parameters except LDL-C with regard to glycemic control. The severity of dyslipidemia increases in patients with higher glycated albumin (GA) value. Elevated levels of GA and dyslipidemia are independent risk factors of cardiovascular diseases and hence, diabetic patients with elevated GA, HbA1c and dyslipidemia considered as high risk group for cardiovascular disease. Improving glycemic control can reduce the risk of cardiovascular events in diabetes [27].

The present study shows significant correlation between glycated albumin (GA) and various lipid parameters, higher mean values of lipid parameters and significant risk ratio between two groups (≤ 7.0 %. and > 7.0%) of glycated albumin indicating that GA is utilized for screening high risk diabetic patients for early diagnosis of dyslipidemia and timely intervention with lipid lowering drugs.

CONCLUSION

Our Study indicates that glycated albumin (GA) levels reflect a quicker response to short-term changes in diabetes treatment and glycemic control index as well as for early diagnosis of dyslipidemia. There is a demonstrated need for an intermediate glycated albumin (GA) index to monitor dyslipidemia in Type-2 Diabetes. Limitations of the present study must also be considered. As our study was not based on the general population, selection bias might have affected the outcome of the study. Larger sample size in general population may be required to confirm the results of the present study.

ACKNOWLEDGEMENT

The authors are thankful to the Management, Mr. M. Sachithanandam, Vishnu Diagnostics Center, No. 1 Ennakara street, Kanchipuram, 631501, Tamilnadu for providing the necessary facilities and permitting to carry out this research work. Also the authors are also very much thankful to all the Physicians who had referred the cases to this Diagnostic Center.

REFERENCES

1. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus, Diabetes Care, 2011, 34, 62-69.

2. Ramachandran A, Snehalatha C, Current scenario of diabetes in India, J. Diabetes, 2009, 1(1), 18-28.

3. Berry C, Tardif JC, Bourassa MG, Coronary heart disease in patients with diabetes: part I: recent advances in prevention and noninvasive management, *J. Am. Coll. Cardiol,* 2007, 49, 631-42.

4. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance. In: Gan D, Diabetes Atlas. International Diabetes Federation, 3rd ed. Belgium: International Diabetes Federation, 2006, p.15-103.

5. Abate N, Chandalia M, Ethnicity and type-2 diabetes: focus on Asian Indians, *J. Diabetes Complications,* 2001, 15, 320-27.

6. Sultan A, Thuan JF, Avignon A, Primary prevention of cardiovascular events and type-2 diabetes: should we prioritize our interventions?, *Diabetes Metab,* 2006, 32, 559-67.

7. Arshag D Mooradian, Dyslipidemia in type-2 diabetes mellitus, *Nature Clinical Practice Endocrinology and Metabolism,* 2009, 5(3), 150-59.

8. Ayaz K M, Ravindra M, Vivek R, Joshi P, Gopalakrishna Bhat, A study on APO B100/APO A-I Ratio in uncontrolled type-2 diabetes mellitus, *Int. J. Appl. Biol. Pharma. Tech*., 2011, 2(1), 379-84.

9. Koenig RJ, Peterson CM, Jones RL, Correlation of glucose regulation and hemoglobin A1c in diabetes mellitus, N. Eng. J. Med., 1976, 295, 417-420.

10. Dunn PJ, Cole RA, Soeldner JS, Temporal relationship of glycosylated hemoglobin concentrations to glucose control in diabetes, Diabetologia, 1979, 17, 213-220.

11. Rohlfing CL, Wiedmeyer HM, Little RR, defining the relationship between plasma glucose and HbA1c: analysis of glucose profiles and HbA1c in the Diabetes Control and Complications Trials, Diabetes Care, 2002, 25, 275-278.

12. Dolhofer R, Wieland OH, Increased glycosylation of serum albumin in diabetes mellitus, Diabetes, 1980, 29, 417-422.

13. Kennedy L, Mehl TD, Riley WJ, Merimee TJ, Non enzymatically glycosylated protein in diabetes mellitus: an index of short term glycaemia, Diabetologia, 1981, 21, 94-98.

14. Tahara Y, Shima K, Kinetics of HbA1c, glycated albumin and fructosamine and analysis of their weight functions against preceding plasma glucose level, Diab Care, 1995, 18, 440-447.

15. Paroni R, Ceriotti F, Galanello R, Performance characteristics and clinical utility of an enzymatic method for the measurement of glycated albumin in plasma, Clin Biochem, 2007, 40, 1398-1405.

16. Kouzuma T, Usami T, Yamakoshi M, An enzymatic method for the measurement of glycated albumin in biological samples, Clin Chim Acta, 2004, 324, 61-71.

17. Kouzuma T, Study of glycated amino acid elimination for an improved enzymatic glycated albumin measurement method, Clin. Chim. Acta, 2004, 346, 135-143.

18. Jacobs NJ, Van Denmark PJ, Enzymatic determinationof serum triglyceride, *Biochem Biophys,* 1960, 88, 250-55.

19. Gordon T and Gordon M, Enzymatic method to determine the serum HDL-cholesterol, *Am. J. Med,* 1977, 62, 707-08.

20. Friedewald WT, Levy RI and Fredrickson DS, Estimation of the concentration of LDL-cholesterol, *Clin. Chem,* 1972, 18(6), 499-15.

21. Trinder P, Determination of blood glucose using 4-aminophenazone as oxygen acceptor, *J. Clin. Path* 1969, 22, 246.

22. Wexler DJ, Grant RW, Meigs JB, Nathan DM, Cagliero E, Sex disparities in treatment of cardiac risk factors in patients with type-2 diabetes, *Diabetes Care,* 2005, 28, 514-20.

23. Goldberg IJ, Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis, *J. Lipid. Res,* 1996, 37, 693-707.

24. Tavangar K, Murata Y, Pedersen ME, Goeres JF, Hoffman AR, Kraemer FB, Regulation of lipoprotein lipase in the diabetic rat, *J. Clin. Invest*. 1992, 90, 1672-78.

25. Ito C, Maeda R, Ishida S, Sasaki H, Harada H, Correlation among fasting plasma glucose, two hour plasma glucose levels in OGTT and HbA1c, *Diabetes Res Clin Pract,* 2000, 50, 225-30.

26. Ohta T, Nishiyama S, Nakamura T, Saku K, Maung K K, Matsuda I, Predominance of large low density lipoprotein particles and lower fractional esterification rate of cholesterol in high density lipoprotein in children with insulin dependent diabetes mellitus, *Eur J Pediatr,* 1998, 157, 276-81.

27. Khan HA, Sobki S H, Khan S A. Association between glycemic control and serum lipid profile in type-2 diabetic patients: HbA1c predicts dyslipidemia, *Clin. Exp. Med.* 2007, 7, 24-29.

Source of support: Nil
Conflict of interest: None Declared