International Journal of Medical and Health Research
ISSN: 2454-9142
www.medicalsciencejournal.com
Volume 4; Issue 9; September 2018; Page No. 161-164

Comparative study of glycated haemoglobinhba1c and lipid profile in diabetic patients

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Abstract
It has been recognized for several decades that diabetes mellitus is an established risk factor for atherosclerotic cardiovascular, cerebrovascular and peripheral vascular morbidity and mortality. Coronary artery disease (CAD) is multifactorial in etiology and has several important risk factors, out of which diabetes is one of the important modifiable risk factor. Dyslipidaemia is one of the important diabetic complications which is a classical risk factor for cardiovascular disease. Based on above findings the study has planned to assess the level of HbA1c and lipid profile in patients with diabetic complications and compare with patients without complications.
Total 25 patients suffered from diabetes were enrolled in the present study. The study was planned in the Department of Biochemistry in Patna Medical College from Oct 2015 to Sept 2016. The age group of the patients are from 30-70 years. The patients visited to Out Patient Department (OPD) and in-patient department (IPD) of a tertiary care hospital were considered in the study. The biochemical parameters like Fating glucose level, Glycated haemoglobin (HbA1c), Total cholesterol, Triglycerides, High Density Lipid, and Low Density Lipid were estimated. Also the electrolyte levels like sodium, potassium, chlorine and bicarbonate is also monitored.
It was concluded from the results of this study that HbA1c can be used as a predictor of dyslipidaemia in type 2 diabetics in addition to as glycaemic control parameter. Thus, early diagnosis of dyslipidaemia can be used as a preventive measure for the development of cardiovascular disease (CVD) in type 2 diabetics.

Keywords: diabetes, HbA1c, lipid profile

Introduction
HbA1c refers to glucose and haemoglobin joined together (the haemoglobin is 'glycated'). Haemoglobin is the protein in red blood cells that carries oxygen throughout your body. The amount of HbA1c formed is directly related to the amount of glucose in your blood.
Glycated haemoglobin (haemoglobin A1c, HbA1c, A1C, or less commonly HgbA1c, haemoglobin A1c, HbA1c, Hb1c, etc.) is a form of haemoglobin that is covalently bound to glucose. It is formed in a non-enzymatic glycation pathway by haemoglobin 's exposure to plasma glucose. It is measured primarily to identify the three-month average plasma glucose concentration and thus can be used as a diagnostic test for diabetes and as assessment test for glycaemic control in people with diabetes [1]. The test is limited to a three-month average because the lifespan of a red blood cell is four months (120 days). However, since red blood cells do not all undergo lysis at the same time, HbA1C is taken as a limited measure of three months. HbA1c is a measure of the beta-N-1-deoxy fructosyl component of haemoglobin [2]. The origin of the naming derives from Haemoglobin type A being separated on cation exchange chromatography. The first fraction to separate, probably considered to be pure Haemoglobin A, was designated HbA0, the following fractions were designated HbA1a, HbA1b, and HbA1c, respective of their order of elution. There have subsequently been many more sub fractions as separation techniques have improved [3]. Normal levels of glucose produce a normal amount of glycated haemoglobin. As the average amount of plasma glucose increases, the fraction of glycated haemoglobin increases in a predictable way. This serves as an indicator that blood sugar is increasing and that action should be taken.
In diabetes mellitus, higher amounts of glycated haemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy, neuropathy, and retinopathy. A trial on a group of patients with Type 1 diabetes found that monitoring by caregivers of HbA1c led to changes in diabetes treatment and improvement of metabolic control compared to monitoring only of blood or urine glucose [4]. However, a trial designed specifically to determine whether reducing HbA1c below the normal 6%, using primarily insulin and sulfonylureas (both known to easily drive blood sugar too low), would reduce the rate of cardiovascular events in type 2 diabetes found higher mortality—the trial was terminated early [5]. The negative outcomes may well have been a result of the treatment approach, primarily insulin and sulfonylureas, utilized in the "intensive" treatment group instead of LCHF (Low-Carbohydrate High Fat diet), GlP-1 analogues & SGLT-2 inhibitors, none of which have these problems & lower cardiovascular mortality.

Glycation of proteins is a frequent occurrence, but in the case of haemoglobin, a nonenzymatic condensation reaction occurs between glucose and the N-end of the beta chain. This reaction produces a Schiff base (R-N=CHR', R = beta chain, CHR'= glucose-derived), which is itself converted to 1-deoxyfructose. This second conversion is an example of an Amadori rearrangement.

When blood glucose levels are high, glucose molecules attach to the haemoglobin in red blood cells. The longer hyperglycaemia occurs in blood, the more glucose binds to haemoglobin in the red blood cells and the higher the glycated haemoglobin. Once a haemoglobin molecule is glycated, it remains that way. A buildup of glycated haemoglobin within the red cell, therefore, reflects the average level of glucose to which the cell has been exposed during its life-cycle. Measuring glycated haemoglobin assesses the effectiveness of therapy by monitoring long-term serum glucose regulation.

A1c is a weighted average of blood glucose levels during the life of the red blood cells (117 days for men and 106 days in women. Therefore, glucose levels on days nearer to the test contribute substantially more to the level of A1c than the levels in days further from the test [6]. This is also supported by data from clinical practice showing that HbA1c levels improved significantly after 20 days from start or intensification of glucose-lowering treatment [7].

Glycosylated haemoglobin (HbA1c) is the most vital target of glycaemic control. The desirable value for HbA1c is values below 7.00 5-7. HbA1c is important standard in analysis of patients' status that indicates the average blood glucose during the past three months which is essential to ensure the optimal care of diabetic patients. The research has revealed that with each one percent reduction in the value of HbA1c, the risk of microvascular complications is reduced by 40 percent.

It has been recognized for several decades that diabetes mellitus is an established risk factor for atherosclerotic cardiovascular, cerebrovascular and peripheral vascular morbidity and mortality. Coronary artery disease (CAD) is multifactorial in etiology and has several important risk factors, out of which diabetes is one of the important modifiable risk factor. Dyslipidaemia is one of the important diabetic complications which is a classical risk factor for cardiovascular disease [8].

Based on above findings the study has planned to assess the level of HbA1c and lipid profile in patients with diabetic complications and compare with patients without complications.

Materials & Methodology

Total 25 patients suffered from diabetes were enrolled in the present study. The study was planned in the Department of Biochemistry in Patna Medical College From Oct 2015 to Sept 2016. The age group of the patients are from 30-70 years. The patients visited to Out Patient Department (OPD) and in-patient department (IPD) of a tertiary care hospital were considered in the study.

The biochemical parameters like Fating glucose level, Glycated haemoglobin (HbA1c), Total cholesterol, Triglycerides, High Density Lipid, and Low Density Lipid were estimated. Also the electrolyte levels like sodium, potassium, chlorine and bicarbonate is also monitored.

The 25 patients were enrolled into the group A as Diabetic patients and 25 patients were considered in the Group B as controlled study patients without any complications.

The approval of the institutional ethics committee was taken before starting the study. All the patients and their parents were informed consents. The aim and the objective of the present study were conveyed to them.

Following was the inclusion and exclusion criteria of the study:

Inclusion Criteria

- Patients admitted with Acute Myocardial Infarction including both ST elevation (STEMI) and non ST elevation (NSTEMI) myocardial infarction.

Exclusion Criteria

- Patients with thyroid disorder
- Pregnancy
- Diabetic Nephropathy
- Patients with chronic illness.
- Patients with Type-1 diabetes mellitus
- Patients on hormone replacement therapy
- Patients on steroids

Results & Discussion

Data from the two study groups patients were collected and presented as below. The 25 patients were enrolled into the group A as Diabetic patients and 25 patients were considered in the Group B as controlled study patients without any complications.

Table 1: Demographic Details

		Group A	Group B
Parameter		**Diabetic patients**	**Controlled study patients**
Sex	Male	15	19
	Female	10	06
	Total	25	25
Age	20-30 years	0	1
	30-40 years	5	6
	40-50 years	6	5
	51- 60 years	7	4
	61- 70 years	7	9
	Total	25	25

Table 2: Comparison of Bio Chemical Parameter in 2 study groups

Group	Group A	Group B
Bio Chemical Parameter	**Diabetic patients**	**Controlled study patients**
Fating glucose level (mg%)	165.3 ± 18.5	90.2 ± 15.6
Glycated haemoglobin (HbA1c) (%)	8.5±2.5	5.9± 0.8
Total cholesterol (mg%)	186.9 ±35.9	160.8± 29.8
Triglycerides (mg%)	196.6 ± 50.5	175.8 ± 45.6
High Density Lipid (mg%)	43.4 ± 7.6	48.5 ± 8.3
Low Density Lipid (mg%)	93.6 ± 28.0	110.2 ±32.8

The concentration of HbA1c, Cholesterol and low density lipid implies a positive correlation with the triglycerides. The levels of the high density lipid and serum chlorine showed negative correlation with triglycerides. Cholesterol and low density lipid showed significant positive correlation with HbA1c. The bicarbonate showed a significant positive correlation with high density lipid. The low density lipid showed a positive correlation with cholesterol.

In recent days the major advances in the treatment of acute coronary syndromes (ACS) have had a significant impact on morbidity and mortality of patients with acute myocardial infarctions (AMI).Nevertheless, Diabetes continues to put patients with and without a prior history of myocardial infarction at significant cardiovascular risk. In the Framingham Heart Study, it was seen that the presence of diabetes doubled the age-adjusted risk of cardiovascular disease in men and tripled it in women. Diabetes remained an independent risk factor even after adjusting for age, hypertension, smoking and left ventricular hypertrophy [10].

The mechanisms by which hyperglycemia and dyslipidemia cause diabetic vascular diseases are the formation and accumulation of advanced glycation end products (AGEs), increased oxidative stress, activation of protein kinase C (PKC), increased flux through the hexosamine pathway, vascular inflammation, deficiency of insulin action in the vasculature, and altered expression and action of hormones, growth factors, and cytokines [11]. In addition, chemical modification of lipoprotein in diabetic states, including peroxidation and glycation, may be an underlying pathogenic mechanism linking dyslipidemia to diabetic complications. For instance, oxidation may increase atherogenicity of the lipoproteins, whereas glycation may enhance the oxidative stress of the lipoproteins. Furthermore, chemical modification of proteins by lipids, such as formation of lipoxidation end products, has also been suggested to be a likely pathogen for vascular changes in diabetes [12].

Results of this study show that the levels of LDL, HDL, TC and TG were significantly higher in type 2 diabetics. These findings were in agreement with the previous studies [13]. High prevalence of hypercholesterolemia, hypertriglyceridemia and high LDL and low HDL was found in type 2 diabetics in this study which are well known risk factors for cardiovascular diseases. Goldberg (1996) [14] reported that the cause of dyslipidaemia in type 2 diabetes mellitus may be that insulin is not working properly which affects the liver Apo lipoprotein production. The Apo lipoprotein regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein (Goldberg, 1996). A highly positive significant relationship of HbA1c with dyslipidemia was observed in the present study. Erciyas *et al*, [15] also reported positive correlation of HbA1c level with TC and TG in diabetic patients.

We also conclude that HbA1c predicts serum lipid profile. It provides valuable supplementary information about the extent of circulating lipids. Thus, dual biomarker capacity of HbA1c (glycaemic control as well as lipid profile indicator) may be utilized for screening high-risk diabetic patients for timely intervention with lipid lowering drugs and thus preventing adverse cardiovascular events.

Conclusion

It was concluded from the results of this study that HbA1c can be used as a predictor of dyslipidaemia in type 2 diabetics in addition to as glycemic control parameter. Thus, early diagnosis of dyslipidaemia can be used as a preventive measure for the development of cardiovascular disease (CVD) in type 2 diabetics.

References

1. Use of Glycated Haemoglobin (HbA1C) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation. Geneva: World Health Organization.. 2, Glycated haemoglobin (HbA1c) for the diagnosis of diabetes. Retrieved, 2011-2018.
2. Miedema K. Standardization of HbA1c and Optimal Range of Monitoring. Scandinavian Journal of Clinical and Laboratory Investigation. 2005; 240:61-72. doi:10.1080/00365510500236143. PMID 16112961.
3. Peterson KP, Pavlovich JG, Goldstein D, Little R, England J, Peterson CM. What is hemoglobin A1c? An analysis of glycated hemoglobins by electrospray ionization mass spectrometry. Clinical Chemistry. 1998; 44(9):1951-58. PMID 9732983.
4. Larsen ML, Hørder M, Mogensen EF. Effect of long-term monitoring of glycosylated haemoglobin levels in insulin-dependent diabetes mellitus". N. Engl. J. Med. 1990; 323(15):1021-25. doi:10.1056/NEJM199010113231503. PMID 2215560.
5. Gerstein HC, Miller ME, Byington RP, *et al*. Effects of Intensive Glucose Lowering in Type 2 Diabetes. New England Journal of Medicine. 2008; 358(24):2545–59. doi:10.1056/NEJMoa0802743. ISSN 0028-4793. PMC 4551392. PMID 18539917.
6. Unnikrishnan, Ranjit. Drugs affecting HbA1c levels. Indian Journal Endocrinol Metabolism. 2012; 16(4):528-531. doi:10.4103/2230-8210.98004.

7. Sidorenkov G, Haaijer-Ruskamp FM, de Zeeuw D, Denig P. A longitudinal study examining adherence to guidelines in diabetes care according to different definitions of adequacy and timeliness". PLoS ONE. 2011; 6(9):e24278.
8. Abdulbari Bener, Mahmoud Zirie, Mohammed H. Daghash Lipids, lipoprotein(a) profile and HbA1c among Arabian Type2 diabetics. Biomedial research. 2007; 18:97-102.
9. Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998; 339:229-34.
10. Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem. 2002; 48:436-472.
11. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA. 2002; 287:2570-2581.
12. Pansuria M, Xi H, Li L, Yang XF, Wang H. Insulin resistance, metabolic stress, and atherosclerosis. Front Biosci (Schol Ed). 2012; 4:916-931.
13. 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; 28:514-520.
14. Goldberg I.J. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. J. Lipid Res. 1996; 37:693-707.
15. Erciyas F, Taneli F, Arslan B, Uslu Y. Glycemic control, oxidative stress and lipid profile in children with type 1 Diabetes Mellitus. Arch. Med. Res. 2004; 35:134-140.