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Research Article

Role of Glycosylated Haemoglobin in Diabetic Patients associated with Hyperlipidemia in Chhattissgarh Region: A Biochemical Analysis

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ABSTRACT
Diabetes has not yet been systematically studied and the role of Glycosylated haemoglobin (HbA1c) on diabetes associated hyperlipidemia gains less attention in Chhattisgarh region of India. Hence, the role of HbA1c in diabetes associated hyperlipidemia in Chhattisgarh was investigated. The study was undertaken including both male and female subjects and the fasting blood sugar, post prandial blood sugar, HbA1c, total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) were analyzed in the blood. The results showed that the fasting, post prandial blood sugar, HbA1c, TC, TG and LDL levels increased significantly in diabetes associated hyperlipidemia. However, there was significant decrease in HDL levels in diabetes associated hyperlipidemia. Therefore, the present study leads to a conclusion that a good glycemic control by monitoring HbA1c would be the useful tool to reduce the pathogenesis of diabetic complications.
Keywords:

1. INTRODUCTION

Diabetes have been increasing worldwide, is a serious debilitating and deadly disease that has now reached epidemic proportion and the prevalence rates are expected to go even higher in the fore seeable future. It has been estimated that the number of adults affected by diabetes in the world will grow from 135 million in 1995 to 300 million in the year 2025. The prevalence of diabetes is higher in developed than in developing countries, but the major increase in people with diabetes will occur in developing countries. Countries like India, China, and the U.S. are currently with the largest number of people with diabetes[1].

The long-term complications of diabetes arises a critical problem for individuals and health care providers. To access the long-term complications of diabetes a regular monitoring of blood glucose is required. It has been suggested that the good glycemic control is more potent factor and is being assessed by the measurement of glycosylated haemoglobin[2] (HbA1c). Further, this assay plays a central role in diabetic management, patient clinical guidance etc. It has been recognized that the blood glucose estimation is a prime test for optimizing treatment schedule of diabetes mellitus. However, the HbA1c estimation is found to be a new and better method to monitor the long-term glucose control irrespective of glucose measurement for patient management. It would prevent or delay the further diabetic complications. Furthermore, it has been recommended by American Diabetes Association that the diabetic patients who will follow oral anti-hyperglycemic therapy should go for HbA1c test[3]. It has been widely accepted that the HbA1c is used as the most reliable test for assessing chronic glycemia[4]. Additionally, HbA1c reflects overall blood glucose levels over a period of 2-3 months and is used to monitor diabetic treatment[5]. The major use of the HbA1c assay is to assess changes in metabolic control that follow an alteration in diabetes treatment. Diabetes treatment is adjusted based on the HbA1c results, expressed as the percentage of haemoglobin that is glycated[6]. It has been reported that the HbA1c does not require fasting blood sample and it is not affected by recent meals[5]. Literature review suggests that HbA1c levels are associated with other risk factors for cardiovascular disease and diabetes, including low birth weight[7]. Therefore, a regular measurement of HbA1c is now recognized as an essential adjunct to self-blood glucose estimation in the achievement of the best possible glycemic control.

Abnormal lipid metabolism is a most common and predominant in diabetic patients. It has been studied that the most diabetic patients (65-80%) die with cardiovascular complications[8] and further there is a high risk for diabetic women compared to non-diabetic population[9]. In USA, mortality from heart disease has

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declined in the general population, but not among diabetic patients[10]. Thus, type-2 diabetes represents an important cardiovascular risk factor[11]. Coronary heart disease (CHD) in diabetic patients is associated with numerous pathological features, including hypertension, hyperglycemia, dyslipidemia, endothelial dysfunction, micro-vascular disease, autonomic neuropathy, abnormal HbA1c levels and defects in cardiac structure and function[12]. The excess of risk of CHD in patients with diabetes is not fully explained, but dyslipidemia is likely to be a major contributor. It has been reported that the prevalence of raised total cholesterol concentration in type-2 diabetes is similar to that in general population however, subjects with type-2 diabetes show the characteristic lipid profile of normal or only slightly raised low density lipoprotein (LDL) cholesterol; with low high density lipoprotein (HDL) cholesterol; and mild elevation of triglyceride[13].

The elevated triglyceride and reduced HDL cholesterol level is a common feature of patients with type-2 diabetes and predicts a substantially increased risk for CHD[14]. Diabetes dyslipidemia or hyperlipidemia includes multiple lipoprotein disorders[15]. Untreated diabetes can cause severe hyperlipidemia, but lipids are nearly normal in non-obese patients with well controlled diabetic patients[16]. The hyperlipidemia of poorly controlled diabetes is due to insulin insufficiency, and causes excessive production of very low density lipoprotein by the liver and decreased clearance of rich lipoprotein because the lipoprotein lipase is not activated. It has been documented that the elevated levels of LDL cholesterol is responsible for the increased risk of CHD, however it is now evident that the reduced HDL cholesterol and elevated triglyceride concentration may be more important and powerful predictors of CHD in diabetic patients[17].

Therefore, in the present study the role of HbA1c is evaluated in diabetes associated hyperlipidemia. Further, the fasting, post prandial blood sugar level and the lipid profile which includes TC, TG, LDL and HDL levels in blood is estimated.

2. MATERIAL &METHODS

2.1. Subjects:

Both the male and female subjects belonging to different age groups (30 to 70 years), different economic groups (upper, middle and lower), different dwellings (urban, semi-urban, rural), different occupations (professionals, farmers, businessmen and students), from the patients of Chhattisgarh population those who are suffering from the Type-2 Diabetes mellitus. Sample collection was normally carried out during the working hours i.e. in between 8.00 am to 5.30 pm. every day. A consent letter has been taken form all the subjects and the experiment is approved by Institution Ethics Review Board, Chhattisgarh Institute of Medical Science, Bilaspur, India.

2.2. Chemicals and Reagents:

All chemicals and reagents of Excellar quality of Roche diagnosis Ltd., (Germany and USA), Randox (UK), Bayer & Accurex (India) have been used for various chemical analyses and estimations.

2.3. Experimental Design:

The study was undertaken in 160 diabetic patients during 2007-09 including both male and female subjects. The experiment was carried out in four different groups and was divided into control, diabetes (DM), hyperlipidemia (HL) and diabetes associated hyperlipidemia (DM+HL) groups. The over all mean values have been determined for 20 diabetic patients in the period of two years including 20 control patients values were subjected for statistical analysis.

2.4. Sample Collection:

The blood samples were collected in the morning on fasting (8-12 hrs fasting after their dinner the previous night) and postprandial (1½. hrs. to 2 hrs after lunch). The same procedure was followed for each patient on his/her every visit. The Hb1Ac was estimated in EDTA anti-coagulated specimen, as it has to be done in the whole blood with preparation of haemolysate sample, while other parameters were estimated in serum or plasma samples. Special care was taken during sample collection from different patients to maintain and keep up time.

2.5. Biochemical estimation:

The fasting and post prandial blood sugar, TC, TG, LDL and HDL were estimated by following end point colorimetric assay method[18] and the Hb1Ac was estimated by following Turbidometric inhibition Immuno assay method[19]. All the readings were taken by using Hitachi-912 fully automatic chemical analyzer.

2.6. Statistical analysis:

The results are expressed as Mean ± S.E.M. The statistical significance was determined by One-Way Analysis of Variance (ANOVA) followed by *Post-hoc* Student Newman Keuls test. $P < 0.05$ was considered to be statistically significant.

3. RESULT

3.1. Effect on fasting blood sugar levels:

The effect of fasting blood sugar level is illustrated in Fig-1. Statistical analysis by One way ANOVA revealed that there was significant difference among groups [$F(3, 76) = 2.75$, $P<0.05$]. *Post hoc* analysis by Student Newmann keuls test revealed that diabetes (DM) and diabetes associated hyperlipidemia (DM+HL) groups were significantly increased fasting blood sugar levels and no significant change in fasting blood sugar levels was observed in hyperlipidemic (HL) group compared to control. Further, there was significant decrease in fasting blood sugar in HL and was found to be no significant change in fasting blood sugar levels in DM+HL compared to DM, indicating that hyperlipidemia has no role in the levels of fasting blood sugar of both control and diabetic subjects. Furthermore, DM+HL showed significant increase in fasting blood sugar levels in fasting blood sugar level compared to HL.

Fig. 1.

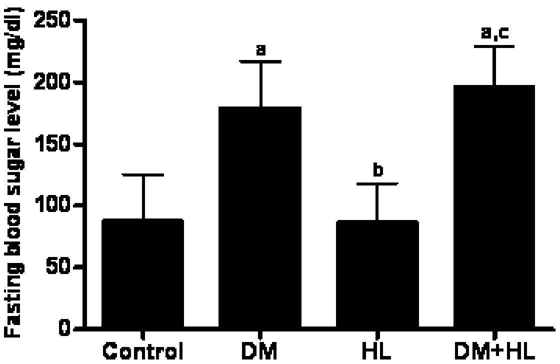

Fig. 1. The effect on fasting blood sugar level is depicted in control, diabetes (DM), hyperlipidemia (HL) and diabetes associated hyperlipidemia (DM+HL). All values are Mean±SEM. [a]P<0.05 compared to control, [b]P<0.05 compared to DM and [c]P<0.05 compared to HL [One-way ANOVA followed by Student Newmann keuls test]

3.2. Effect on post prandial blood sugar level:

Fig-2 depicts the effect on post prandial blood sugar levels. Statistical analysis by One way ANOVA revealed that there was significant difference among groups [F (3, 76) = 2.68, P<0.05]. *Post hoc* analysis by Student Newmann keuls test revealed that diabetes (DM)

Fig. 2.

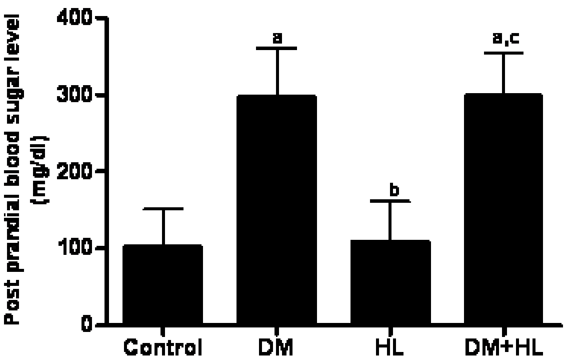

Fig. 2. The effect on post prandial blood sugar level is illustrated in control, DM, HL and DM+HL. All values are Mean±SEM. [a]P<0.05 compared to control, [b]P<0.05 compared to DM and [c]P<0.05 compared to HL [One-way ANOVA followed by Student Newmann keuls test].

and diabetes associated hyperlipidemia (DM+HL) groups were significantly increased in post prandial blood sugar levels and no significant change in post prandial blood sugar levels was observed in hyperlipidemic (HL) group compared to control. Further, there was significant decrease in post prandial blood sugar levels in HL and was found to be no significant change in post prandial blood sugar levels in DM+HL compared to DM, indicating that hyperlipidemia has no role in the levels of post prandial blood sugar levels of both control and diabetic subjects which mimics the effect of fasting blood sugar levels. Furthermore, DM+HL showed significant increase in post prandial blood sugar levels compared to HL.

Fig. 3.

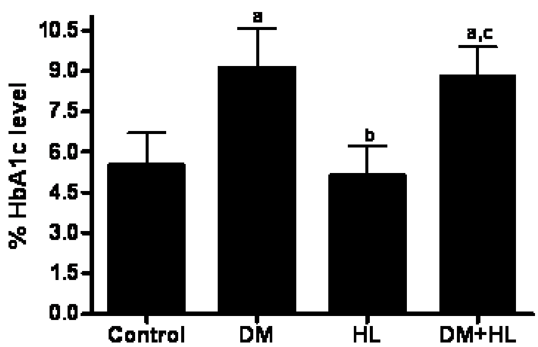

Fig. 3. The effect on Hb1Ac level is illustrated in control, DM, HL and DM+HL. All values are Mean±SEM. [a]P<0.05 compared to control, [b]P<0.05 compared to DM and [c]P<0.05 compared to HL [One-way ANOVA followed by Student Newmann keuls test].

3.3. Effect on glycosylated hemoglobin (Hb1Ac) level in blood:

The effect of Hb1Ac levels is illustrated in Fig-3. Statistical analysis by One way ANOVA revealed that there was significant difference among groups [F (3, 76) = 3.02, P<0.05]. *Post hoc* analysis by Student Newmann keuls test revealed that diabetes (DM) and diabetes associated hyperlipidemia (DM+HL) groups were significantly increased in Hb1Ac levels and no significant change in Hb1Ac levels was observed in hyperlipidemic (HL) group compared to control. Further, there was significant decrease in Hb1Ac levels in HL and was found to be no significant change in Hb1Ac levels in DM+HL compared to DM, indicating that hyperlipidemia has no role in the levels of Hb1Ac levels of both control and diabetic subjects which mimics the effect of both fasting blood sugar and post prandial blood sugar levels. Furthermore, DM+HL showed significant increase in Hb1Ac levels compared to HL.

3.4. Effect on Total cholesterol (TC) in blood:

Fig-4 depicts the effect on TC levels. Statistical analysis by One way ANOVA revealed that there was significant difference among groups [F (3, 76) = 3.14, P<0.05]. *Post hoc* analysis by Student Newmann keuls test revealed that HL and DM+HL showed significant increase in TC level in blood compared to both control and DM groups, indicating enhanced lipid profile.

3.5. Effect on Triglyceride (TG):

The effect on TG levels is illustrated in Fig-5. Statistical analysis by One way ANOVA revealed that there was significant difference among groups [F (3, 76)

Fig. 4.

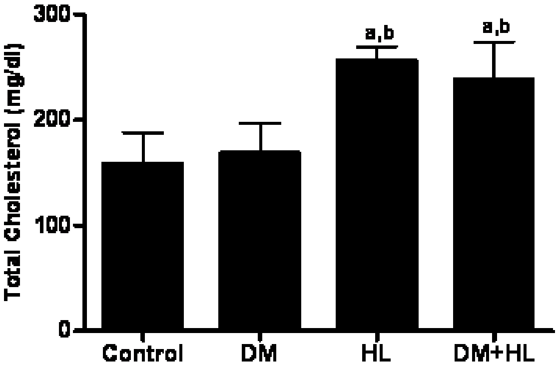

Fig. 4. The effect on Total cholesterol level in blood is illustrated in control, DM, HL and DM+HL. All values are Mean±SEM. [a]P<0.05 compared to control and [b]P<0.05 compared to DM [One-way ANOVA followed by Student Newmann keuls test].

= 4.29, P<0.05]. *Post hoc* analysis by Student Newmann keuls test revealed that HL and DM+HL showed significant increase in TG level in blood compared to both control and DM groups, indicating over activity of lipid profile.

Fig. 5.

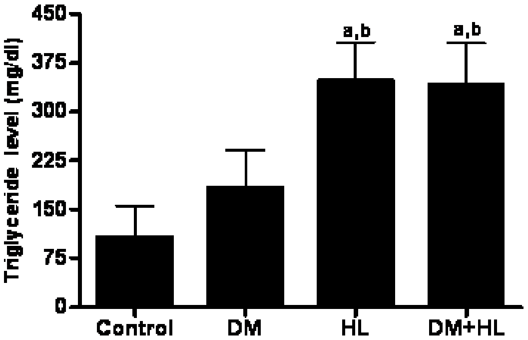

Fig. 5. The effect on Triglyceride level in blood is illustrated in control, DM, HL and DM+HL. All values are Mean±SEM. [a]P<0.05 compared to control and [b]P<0.05 compared to DM [One-way ANOVA followed by Student Newmann keuls test].

3.6. Effect on LDL level:

Fig-6 depicts the effect on LDL levels. Statistical analysis by One way ANOVA revealed that there was significant difference among groups [F (3, 76) = 3.23, P<0.05]. *Post hoc* analysis by Student Newmann keuls test revealed that HL and DM+HL showed significant increase in LDL level in blood compared to both control and DM groups, indicating augmented lipid profile.

3.7. Effect on HDL level:

The effect on HDL levels is depicted in Fig-7. Statistical analysis by One way ANOVA revealed that there was significant difference among groups [F (3, 76) = 8.22, P<0.05]. *Post hoc* analysis by Student Newmann keuls test revealed that there was a significantly reduced level of HDL in the blood of DM and DM+HL subjects compared to control. Further, HL and DM+HL subjects showed significant elevated levels of HDL in the blood compared to DM. Furthermore, there were significant reduced levels in the HDL of DM+HL subjects compared to HL group.

Fig. 6.

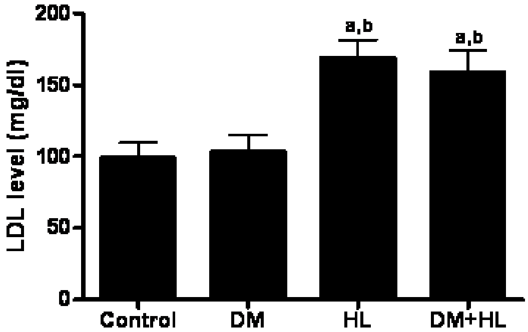

Fig. 6. The effect on Low density lipoprotein (LDL) level in blood is depicted in control, DM, HL and DM+HL. All values are Mean±SEM. [a]P<0.05 compared to control and [b]P<0.05 compared to DM [One-way ANOVA followed by Student Newmann keuls test].

Fig. 7.

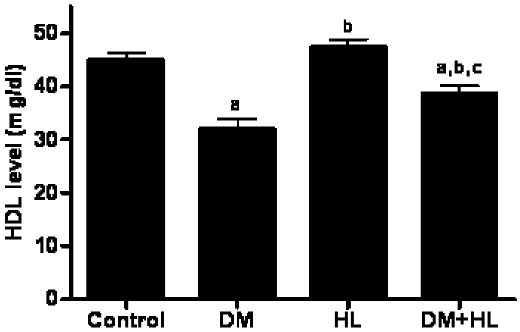

Fig. 7. The effect on High density lipoprotein (HDL) level in blood is depicted in control, DM, HL and DM+HL. All values are Mean±SEM. [a]P<0.05 compared to control, [b]P<0.05 compared to DM and [c]P<0.05 compared to HL [One-way ANOVA followed by Student Newmann keuls test].

4. DISCUSSION

In the present investigation, diabetes associated hyperlipidemia (DM+HL) showed significant elevated levels of HbA1c in blood. Further, elevated levels of fasting and post prandial sugar in blood of DM+HL was observed. Furthermore, the TC, TG and LDL levels were elevated in the blood of DM+HL; however there were reduced levels of HDL in the blood of DM+HL. The present study gains critical importance as HbA1c is an important tool in clinical investigation and would guide in the pathophysiological development of DM+HL.

HbA1c level was elevated in the blood of both DM and DM+HL subjects. It has been reported that the diabetic patients possess elevated level of Hb1Ac[20] which is in agree with our present findings. The diabetic subjects with HbA1c may create various clinical situations for the development of diabetes complications. The present findings suggest that there was a strong relationship between fasting, post-prandial blood sugar and HbA1c level in diabetic patients. Black has similarly reported that the blood glucose and HbA1c levels considerably increased in diabetic patients[21]. Further, it has been reported from another study that there is elevated levels of fasting sugar, post prandial sugar and Hb1Ac in diabetes associated hyperlipidemia[22]. It has been suggested that there are certain clinical diagnoses and utmost care is required to diabetic patients in order to effectively suppress the severity of diabetes. Here, monitoring of the Hb1Ac was carried out in every three months to maintain proper data for the effective diabetes managements. Thus, HbA1c was observed to play a major role in diabetic complications and in the improvement of good glycemic control.

As evident from the results that a significant correlation existed between HbA1c and serum lipid profile level. The TC, TG and LDL levels were elevated in DM+HL subjects however; HDL levels were reduced in DM+HL subjects. This alteration may be due to poor glycemic state and improperly following of prescribed medicine for diabetes. It can be improved by strict blood glucose control and its steady maintenance of the level of HbA1c and lipid profile in order to prevent the further advancement of complications of diabetes. It is assumed that staying in good control of diabetes over a prolonged period of time requires a recommended meal plan, sticking into a physical activity programme, taking prescribed diabetes medicines, self monitoring of blood glucose if recommended, and consulting a health care provider often. Similar pathological changes have been recommended by earlier worker Gaby[23] who has reported elevated HbA1c and lipid levels in all diabetic related disorders.

Disorders of lipid metabolism were found to be common and predominant in diabetes and there were major risk factors for the high frequency of atheromatous complications in diabetes mellitus. Most patients (65-80%) with type-2 diabetes died from heart disease[8] and diabetic women carry particularly high risk as compared to non-diabetic population. In the USA, mortality from heart disease has declined in the general population, but not among diabetic patients. Thus, type-2 diabetes represents an important cardiovascular risk factor which pre-disposes especially to aggressive CHD that typically affects smaller vessels. CHD in diabetic patients is associated with several pathological features including hypertension, hyperglycemia and abnormal HbA1c, dyslipidemia, endothelial dysfunction, microvascular disease, autonomic neuropathy and defects in cardiac structure and function[24]. The prevalence of elevated TC level in type-2 diabetes is similar to that in the general population however; the incremental risk was higher in the subjects with type-2 diabetes with increased cholesterol than in non diabetic subjects. Further, it has been evident that the hypercholesteremia, hypertriglyceremia and elevated LDL are considered to be powerful predictors for CHD[25]. Hence, management of diabetes with hyperlipidemia begins with lifestyle modification like dietary restriction for the obese, increased physical activities, improved glycemic control and maintenance of blood pressure well controlled and cessation of smoking[26]. It has been reported that in well-controlled diabetic patients, the lipids and lipoproteins levels are similar to non-diabetic subjects, however, in poorly controlled patients, the TC, TG, LDL and VLDL levels were found in elevated conditions while HDL was found in reduced conditions[27].

It is evident that the diabetic patients are more prone to get micro and macro-vascular complications than normal persons. The long-term control is necessary to maintain the level of Hb1Ac in diabetes with hyperlipidemia which may prevent further complications like nephropathy, neuropathy and arteriosclerosis. Further, it has been suggested that the activation of triglyceride lipase was found to alter lipid levels significantly in diabetic patients who considerably recovered with good metabolic control[28]. Similarly, Tomkin, 1994 has reported that the LDL-Cholesterol is strongly related to vascular risk, predominantly in type-2 diabetes and it is well correlated with macrovascular disease in type-1 and type-2 diabetes[29]. In diabetic patients, the low HDL-Cholesterol is a risk factor where as high HDL-Cholesterol appears to safeguard coronary heart disease. The total cholesterol and HDL-cholesterol ratio predicts vascular risk in both sexes. In women when the ratio exceeds 7.5 the susceptibility to coronary heart disease becomes very high. The cardiovascular death rate is increased with increasing cholesterol in both diabetic and non-diabetic patients, but absolute risk was steeper in those with diabetes. Furthermore, Tomkin, 1994 has also concluded that the newer mode of therapy, specifically aimed at normalizing the lipid abnormalities in diabetes includes dietary modifications (e.g. Caloric control, supplementation with monosatuarated fats) and the use of pharmacological agents for lowering triglyceride and cholesterol[29]. All efforts to ensure good glycemic control should be made prior to initiation of drug therapy for hyperlipidemia.

Earlier workers, who has reported that there was a significant decrease in HDL-cholesterol levels in diabetes associated hyperlipidemia which is similar to our findings[30, 31]. Poorly controlled diabetes leads to increased lipolysis and over production of non-esterified fatty acids and decreased activity of lipoprotein lipase. The insulin dependent enzyme, like lipase hydrolyses triglyceride in circulating lipoprotein which leads to hyperlipidemia.

In summary, it is mandatory to perform the Hb1Ac test in various diabetic subjects which may provide various clinical informations and may play pivotal role in preventing the development of genesis of diabetes. Further, it should be carried out for the diabetic management in every 3 months to delay or prevent the advancement of diabetic complications.

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