Content available at: https://www.ipinnovative.com/open-access-journals

International Journal of Clinical Biochemistry and Research

Journal homepage: https://www.ijcbr.in/

Original Research Article

Evaluation of Dyslipidemia with HbA1c levels in Diabetes Mellitus

Aliya Fatima[1], R. D. Malathi[2,*], Mohd Iqbal Ahmed[1]

[1]*Dept. of Biochemistry, Gandhi Medical College, Secunderabad, Telangana, India*
[2]*Dept. of Biochemistry, Kakatiya Medical College, Warangal, Telangana, India*

ARTICLE INFO

Article history:
Received 21-11-2022
Accepted 03-12-2022
Available online 31-12-2022

Keywords:
Diabetes mellitus
Dyslipidaemia
HbA1c

ABSTRACT

Diabetes is a metabolic disease which has hyperglycaemia resulting from defects in insulin secretion or action. HbA1C is one of the most reliable test used for estimation of glycaemic index. Diabetes is often accompanied by undiagnosed dyslipidaemia, characterized by increased triglyceride level, decreased high-density lipoprotein levels and increase in low-density lipoprotein (LDL) particles. Diabetes is a significant risk factor for atherosclerotic cardiovascular disease (ASCVD). The purpose of this study was to correlate lipid parameters with different levels of HbA1c to assess dyslipidaemia with diabetic status.

An observational study was conducted in biochemistry laboratory at Gandhi Hospital, Telangana.

After informed consent, 5ml of venous blood sample was collected in plain tube and EDTA tube from diabetic and apparently non diabetic patients. Estimation of serum triglycerides was done by glycerol phosphate oxidase peroxidase, serum cholesterol by cholesterol oxidase method, serum HDL by direct clearance method in Beckmann Coulter AU 500 and HbA1c was estimated by high performance liquid chromatography in Bio-Rad D10.

A total of 90 samples were divided into 3 groups according to their HbA1c results. Group 1 with HbA1c less than 5.6, Group 2 with HbA1c 5.6-7 and Group 3 with HbA1c more than 7.

The present study showed no variation in the lipid profile in Group 1 with HbA1c < 5.6. In Group 2 with HbA1c between 5.6-7, there was significant increase in LDL cholesterol. In Group 3 with HbA1c >7 there was marked increase in LDL and serum triglyceride. Hence, we can conclude that dyslipidemia is increased in poor glycemic control and evaluation of HbA1c may also be used as a predictor of dyslipidaemia in diabetics.

1. Introduction

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.[1] In 2009, an International Expert Committee recommended that diabetes be diagnosed by measurement of haemoglobin A1c (HbA1c), which reflects long-term blood glucose concentrations.[1]

The blood glucose data available from HbA1c are used in prescribing and monitoring the medicines for diabetes and prediabetes, along with exercise and diet. The accuracy of this test has continued to evolve over the last few years and useful in monitoring the blood glucose values among patients in clinics.[2]

Analysis of glycated haemoglobin (HbA1c) in blood provides evidence about an individual's average blood glucose levels during the previous two to three months, which is the predicted half-life of red blood cells (RBCs).[3] The HbA1c is now recommended as a standard of care (SOC) for testing and monitoring diabetes, specifically the

* *Corresponding author*.
E-mail address: malathi.ramdas@gmail.com (R. D. Malathi).

https://doi.org/10.18231/j.ijcbr.2022.060

type 2 diabetes.[4] With no fasting required and also not being bound by the time of the day on the part of the patient, the HbA1c is a very convenient test to administer and evaluate.[5] The HbA1c is recommended to be performed at least twice a year in diabetes patients with stable blood glucose levels.[6]

The HbA1c levels differ for different diabetes patients, depending on their history of diabetes and whether they are on tablets or long-term and/or short-term insulin dosage.[7] HbA1c is not only a useful biomarker of long-term glycaemic control but also a good predictor of lipid profile; thus, monitoring of glycaemic control using HbA1c could have additional benefits of identifying diabetes patients who are at a greater risk of cardiovascular complications.[8]

Patients with type 2 diabetes often exhibit an atherogenic lipid profile (high TG and low HDL cholesterol) which greatly increases their risk of cardiovascular disease (CVD) when compared with people without diabetes.[9] Significantly higher levels of hypercholesterolaemia and hyperlipidaemia in type 2 diabetic patients with CVD as compared to diabetic patients without CVD have been observed.[10] Interestingly, attempts to reduce cardiovascular risks resulted in the improvement of HbA1c even in the absence of any specific intervention targeted at improving glycaemic control.[11]

Type 2 diabetes is associated with a cluster of interrelated plasma lipid and lipoprotein abnormalities, including reduced HDL cholesterol, a predominance of small dense LDL particles, and elevated triglycerides.[12]

Insulin resistance and type 2 diabetes are associated with a clustering of interrelated plasma lipid and lipoprotein abnormalities, which include reduced HDL cholesterol, a predominance of small dense LDL particles, and elevated triglyceride levels.[12] Each of these dyslipidaemia features is associated with an increased risk of cardiovascular disease. Increased hepatic secretion of large triglyceride-rich VLDL and impaired clearance of VLDL appears to be of central importance in the pathophysiology of this dyslipidemia.[13]

Insulin resistance plays an important role in the development of diabetic dyslipidaemia due to several reasons. In insulin resistance and type 2 diabetes, increased efflux of free fatty acids from adipose tissue and impaired insulin mediated skeletal muscle uptake of free fatty acids increase fatty acid flux to the liver.[13]

Free fatty acid levels are elevated in individuals with impaired glucose tolerance suggests that insulin resistance associated with elevated free fatty acid levels occurs before the onset of hyperglycemia.[13] Epidemiologic studies have also demonstrated a relationship between plasma free fatty acid levels and insulin resistance.[14]

Diabetic patients with accompanied but undiagnosed dyslipidaemia vulnerable to cardiovascular deaths. Patients with type 2 diabetes mostly exhibit an atherogenic lipid profile, which greatly increases their risk of CVD when compared with people without diabetes. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality.[15]

2. Materials and Methods

A case control study was done on 90 patients who were divided into 3 groups of 30 each based on their HbA1c values

Group 1: HbA1c < 5.6 (non diabetic).

Group 2: HbA1c between 5.6 to 7(Good glycemic control)

Group 3: HbA1c > 7 (poor glycemic control)

Willing patients of age group 30-60 yrs with fasting of at least 8 hours before giving the sample were included in the study. Diabetes mellitus patients with known cardiovascular disease, patients with known hypertension and patients with chronic liver disease, kidney disease and thyroid disorders were excluded from study.

A total of 90 samples were included from patients in Outpatient Department of Gandhi Hospital, Secunderabad, after informed consent, 5 mL of venous blood was taken from each patient in EDTA tube and plain tube for HbA1c and lipid profile respectively. Samples were centrifuged at 3500 rpm for 10 minutes and serum was analysed in Biochemistry Department, CDL, Gandhi hospital, Secunderabad.

Analysis of serum lipid profile by enzymatic method which includes Serum triglycerides by enzymatic method (GPO-POD), serum Cholesterol by cholesterol oxidase method, serum HDL by enzymatic- direct immunosuppression method in Beckmann Coulter AU500. Values of VLDL were calculated by the formula TG/5 and LDL by the Friedwald formula LDL= Total Cholesterol-HDL-TG/5. HbA1c was estimated by high performance liquid chromatography on Bio-Rad-D10.

3. Results

A total of 90 samples were taken, which were divided into 3 group according to their HbA1c results.

In the first group of HbA1c<5.6, the following were the Mean ± SD of cholesterol, triglycerides, LDL HDL and, VLDL, as 149.7 ± 40mg/dL, 130.6 ± 59mg/dL, 70.94 ± 33.63mg/dL, 48.03 ± 12.85mg/dL, 25.7 ± 11.94mg/dL respectively. In the second group of samples having HbA1c values between 5.6-7, the mean values for cholesterol, triglycerides, LDL, HDL, VLDL, are 176 ± 56.18mg/dL, 139.72 ± 57.35mg/dL, 108.05 ± 49.37mg/dL, 49.59 ± 33.58mg/dL, 27.79 ± 11.48mg/dL respectively.

In the third group of HbA1c >7 has mean values of cholesterol, triglycerides, LDL, HDL and VLDL as 192.56 ± 60.36mg/dL, 158.09 ± 72.45mg/dL, 126.02 ± 52.36mg/dL, 39.43 ± 7.82mg/dL, 39.43 ± 7.82mg/dL, and 29.65 ± 14.20mg/dL.

Table 1: Comparison of serum cholesterol between the 3 HbA1c study groups

	Group 1	**Group 2**	**Group 3**
HbA1c levels	HbA1c < 5.6	HbA1c: 5.6-7	HbA1c: >7
N	30	30	30
Mean ± SD (mg/dL)	149.7 ± 40.6	176 ± 56.18	192.56 ± 60.36
F-Value	1.23	1.215	2.520
p-value	0.28	0.280	0.124

Table 2: Comparison of serum triglycerides between the 3 HbA1c study groups

	Group 1	**Group 2**	**Group 3**
HbA1c levels	HbA1c < 5.6	HbA1c: 5.6-7	HbA1c: >7
N	30	30	30
Mean ± SD(mg/dL)	130.6 ± 59.0	139.72 ± 57.35	158.09 ± 72.45
F-Value	4.93	0.043	1.042
p-value	0.07	0.837	0.03*

Table 3: Comparison of Serum LDL between the 3 HbA1c study groups

	Group 1	**Group 2**	**Group 3**
HbA1c levels	HbA1c < 5.6	HbA1c: 5.6-7	HbA1c: >7
N	30	30	30
Mean ± SD(mg/dL)	70.94 ± 33.63	108.05 ± 49.37	126.02 ± 52.36
F-Value	0.82	1.621	2.466
p-value	0.37	0.02*	0.022*

Table 4: Comparison of Serum HDL between the 3 HbA1c study groups

	Group 1	**Group 2**	**Group 3**
HbA1C levels	HbA1c < 5.6	HbA1c: 5.6-7	HbA1c: >7
N	30	30	30
Mean ± SD (mg/dL)	70.94 ± 33.63	49.59 ± 33.58	39.43 ± 7.82
F-Value	0.824	1.834	0.247
p-value	0.372	0.187	0.623

Table 5: Comparison of Serum VLDL between the 3 HbA1c study groups

	Group 1	**Group 2**	**Group 3**
HbA1c levels	HbA1c < 5.6	HbA1c: 5.6-7	HbA1c: >7
N	30	30	30
Mean ± SD (mg/dL)	25.71 ± 11.94	27.79 ± 11.48	29.65 ± 14.20
F-Value	4.807	0.028	0.34
p-value	0.37	0.869	0.57

*p<0.05

The p value was calculated by ANOVA method with HbA1c on X axis and lipid parameters on Y axis.

So, from the above results, we can infer that there is significant correlation of LDL with HbA1c values of 5.6-7, as their p value is <0.05 And in case of HbA1c >7 there is significant correlation with LDL and triglycerides as their p values is <0.05. So conclusively we can say that lipid profile parameters like LDL and triglycerides are increased with rise in HbA1c values.

4. Discussion

Lipid abnormalities are frequently observed in patients with type-2 diabetic mellitus in whom there is increased risk of mortality due to associated diabetes complications and therefore require good glycaemic control and lipid parameters.[15]

The abnormal lipid profile in type 2 Diabetes mellitus maybe due to insulin resistance, which causes the increased release of free fatty acids. The Diabetes complications and control trial (DCCT) have identified HbA1c as the gold standard of glycaemic control. It has been suggested that the level of HbA1c ≤7.0% is appropriate to reduce the risk

of cardiovascular complications.[16]

Thambiah et al in their cross-sectional study have shown significant correlation between fasting blood glucose and HbA1c with total cholesterol, triglyceride, low density lipoprotein which emphasises the additional possible use of HbA1c as a biomarker for dyslipidaemia as well as a potential indirect predictor of cardiovascular disease (CVD) risk in T2DM patients.[17] Begum et al in their study have observed that HbA1c can be used as a predictor of dyslipidaemia in type 2 diabetes.[18]

A study of Khan et al in their study indicated that HbA(1c) is not only a useful biomarker of long-term glycaemic control but also a good predictor of lipid profile and therefore monitoring of glycaemic control using HbA(1c) could have additional benefits of identifying diabetic patients who are at a greater risk of cardiovascular complications.[19]

Singh et al. in their study showed HbA1c can be used as a predictor of dyslipidaemia in type 2 diabetics in addition to as glycaemic control parameter, and so early diagnosis of dyslipidaemia can be used as a preventive measure for the development of cardiovascular disease (CVD) in type 2 diabetics.[20]

In a study by Alzahrani et al. it was seen that HbA1c was associated with triglycerides and can be used for early diagnosis of dyslipidaemia.[21] Arshad Hussain et al., in their study showed that apart from a reliable glycaemic index, HbA1c can also be used as a predictor of dyslipidaemia.[22]

In their study Baranwala et al. showed in their study that significant correlation of level of HbA1c with parameters of lipid profile suggests utility of HbA1c as a marker of dyslipidaemia.[23] Reddy S et al. in their diabetic study showed HbA1c can be used in monitoring of long-term glycaemic control and as an indirect indicator of dyslipidaemia in type 2 diabetic patients.[24]

Selvin et al. have demonstrated a linear relationship between CHD and HbA1c in diabetic patients, suggesting that the risk of CHD begins to increase at HbA1c levels even below 7.0%.[25] Grant et al. have reported significantly higher CVD risk factors among individuals with HbA1c>6.0%.[26]

A study from north eastern Indian population investigated the lipid profile and its correlation with HbA1c levels in incidence of myocardial infarction, which concluded that 60% patients with myocardial infarction had poor glycaemic control and found that the serum HbA1c level has direct relationship with the serum lipid profile and is indirectly associated with levels of HDL cholesterol.[27]

A study conducted by Anand et al. established that serum HbA1c levels, adequate glycaemic control, and lipid profile screening help to identify high-risk patients for timely diagnosis of hyperlipidaemia, hence decreases the incidence of cardiovascular diseases and peripheral vascular complications through appropriate interventions.[28]

Mahajan et al. conducted a study, which showed positive correlation of HbA1c with LDL, triglycerides, total cholesterol, high-density lipoprotein, very-low-density lipoprotein, and low-density lipoprotein C levels.[29]

Adninta et al in their study showed a positive correlation between serum triglycerides and HbA1c levels that is high triglyceride levels in groups with HbA1c more than 8 similar to findings in our study.[30]

Syeda Naqvi et al, in their study have divided the study group into 4 according to their HbA1c levels and had correlated serum triglycerides levels with them, which showed positive correlation with groups having HbA1c levels more than 7. Similarly, in the present study triglyceride levels were increased in group with HbA1c more than 7.[31]

Gaurav Gupta et al. in their study have investigated hyperglycaemia and dyslipidaemia in stroke patients through two tier investigation, first by taking a history of medication for anti-diabetic or lipid lowering agents and second by measuring HbA1c and lipid profile with specific importance to LDL levels. This correlation was statistically highly significant suggesting that patients with high HbA1c (more than 6.5) and LDL levels were more likely to have a stroke. They recommended treating diabetes and dyslipidaemia to achieve favourable clinical outcomes. In the present study also, LDL levels were increased in groups with HbA1c more than 5.6.[32]

In United Kingdom Prospective Diabetes Study (UKPDS), it was seen that in patients with type 2 diabetes, the risk of diabetic complications was strongly associated with hyperglycaemia. Glycaemia control with decreased level of HbA1c is likely to reduce the risk of complications.[33]

The above discussion clearly indicates that high HbA1c levels in may indicate dyslipidaemia in diabetes patients, especially those with poor glycaemic control. As prompt interventions can be done to decrease the mortality and morbidity due to complications of diabetes mellitus, HbA1c which is a well-known biomarker of long-term glycaemic control can also be used as a good predictor of lipid profile; thus, monitoring of glycaemic control using HbA1c could have additional benefits of identifying diabetes patients who are at a greater risk of cardiovascular disease.

5. Conclusions

In the present study, significant alteration in the lipid parameters is seen in correlation to the HbA1c levels that is increased LDL and triglyceride levels in patients with poor glycaemic status suggesting the usefulness of HbA1c for screening diabetes patients for dyslipidaemia. As dyslipidaemia and hyperglycaemia are modifiable risk factors, it is recommended that controlling glycaemic index can decrease the dyslipidaemia complications in an individual. However, further research on larger cohorts is

required to provide further evidence for the predictive value of HbA1c for dyslipidaemia.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Rifai N. Diabetes Mellitus. In: Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. Saunders; 2017.
2. Little RR. Glycated haemoglobin standardization-National Glycohemoglobin Standardization Program (NGSP) perspective. *Clin Chem Lab Med*. 2003;41(9):1191–8.
3. Khan MI, Weinstock RS. Carbohydrates. In: McPherson RA, Pincus MR, editors. Henry's Clinical Diagnosis and Management by Laboratory Methods. Philadelphia: Saunders Elsevier; 2011. p. 210–25.
4. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus. Geneva: World Health Organization; 2011. Available from: https://apps.who.int/iris/bitstream/handle/10665/70523/WHO_NMH_CHP_CPM_11.1_eng.pdf.
5. Juarez DT, Demaris KM, Goo R, Mnatzaganian CL, Smith W, H. Significance of HbA1c and its measurement in the diagnosis of diabetes mellitus: US experience. *Diabetes Metab Syndr Obes*. 2014;7:487–94.
6. American Diabetes Association (ADA) Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2011;34:62–9.
7. Bozkaya G, Ozgu E, Karaca B. The association between estimated average glucose levels and fasting plasma glucose levels. *Clinics (Sao Paulo)*. 2010;65(11):1077–80.
8. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. *Clin Exp Med*. 2007;7(1):24–9.
9. Windler E. What is the consequence of an abnormal lipid profile in patients with type 2 diabetes or the metabolic syndrome? *Atheroscler Suppl*. 2005;6(3):11–4.
10. Giansanti R, Rabini RA, Romagnoli F, Fumelli D, Sorichetti P, Boemi M, et al. Coronary heart disease, type 2 diabetes mellitus and cardiovascular disease risk factors: a study on a middle-aged and elderly population. *Arch Gerontol Geriatr*. 1999;29(2):175–82.
11. Woodward A, Wallymahmed M, Wilding J, Gill G. Improved glycaemic control–an unintended benefit of a nurse-led cardiovascular risk reduction clinic. *Diabet Med*. 2005;22(9):1272–4.
12. American Diabetes Association: Management of dyslipidaemia in adults with diabetes (Position Statement). *Diabetes Care*. 2003;26:83–6.
13. Krauss RM. Lipids and Lipoproteins in Patients with Type 2 Diabetes. *Diabetes Care*. 2004;27:1496–1504.
14. Reaven GM, Chen YD. Role of abnormal free fatty acid metabolism in the development of non-insulin-dependent diabetes mellitus. *Am J Med*. 1988;85(5A):106–12.
15. Mahato RV, Gyawali P, Raut PP, Regmi P, Singh KP, Pandeya DR, et al. Association between glycaemic control and serum lipid profile in type 2 diabetic patients: Glycated haemoglobin as a dual biomarker. *Biomed Res*. 2011;22(3):375–80.
16. Farid S. Correlation between HbA1c Values and Lipid Profile in Saudi Type 2 Diabetic Patients. *J Exerc Sci Physiother*. 2017;13(1):1–7.
17. Thambiah SC, Samsudin IN, George E, Sham SYZ, Lee HM, Muhamad MA, et al. Relationship between dyslipidaemia and glycaemic status in patients with Type 2 diabetes mellitus. *Malays J Pathol*. 2016;38(2):123–30.
18. Begum A, Irfan SR, Hoque MR, Habib SH, Parvin S, Malek R, et al. Relationship between HbA1c and Lipid Profile Seen in Bangladeshi Type 2 Diabetes Mellitus Patients Attending BIRDEM Hospital: A Cross-Sectional Study. *Mymensingh Med J*. 2019;28(1):91–5.
19. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomarker Insights*. 2016;11:95–104.
20. Singh G, Kumar A. Relationship among HbA1c and lipid profile in Punajbi type 2 diabetic population. *J Exerc Sci Physiother*. 2011;7(2):99–102.
21. Alzahrani SH, Baig M, Aashi MM, Al-Shaibi FK, Alqarni DA, Bakhamees WH. Association between glycated hemoglobin (HbA1c) and the lipid profile in patients with type 2 diabetes mellitus at a tertiary care hospital: a retrospective study. *Diabetes Metab Syndr Obes*. 2019;12:1639–44.
22. Hussain A, Ali I, Ijaz M, Rahim A. Correlation between haemoglobin A1c and serum lipid profile in Afghani patients with type 2 diabetes: haemoglobin A1c prognosticates dyslipidaemia. *Ther Adv Endocrinol Metab*. 2017;8(4):51–7.
23. Baranwal JK, Maskey R, Majhi S, Lamsal M, Baral N. Association between level of HbA1c and lipid profile in T2DM patients attending diabetic OPD at BPKIHS. *Health Renaissance*. 2003;13(3):16–23.
24. Reddy S, Meera S, William E. Correlation between glycemic control and lipid profile in type 2 diabetic patients: HbA1c as an indirect indicator of dyslipidaemia. *Asian J Pharm Clin Res*. 2014;7(2):153–5.
25. Selvin E, Coresh J, Golden SH, Brancati FL, Folsom AR, Steffes MW. Glycemic control and coronary heart disease risk in persons with and without diabetes: the atherosclerosis risk in community's study. *Arch Intern Med*. 2005;165(16):1910–6.
26. Grant T, Soriano Y, Marantz PR, Nelson I, Williams E, Ramirez D, et al. Community based screening for cardiovascular disease and diabetes using HbA1c. *Am J Prev Med*. 2004;26(4):271–5.
27. Bhattacharjee P, Das P, Nath BK, Basumatary A, Das D. HbA1C and its correlation with lipid profile in acute myocardial infarction. *Int J Contemp Med Res*. 2018;5(4):13–6.
28. Anand. Significance of HbA1c and lipid profile test in diagnosis and prognosis of diabetic and cardio-vascular patients. *Int J Med Heal Res*. 2017;3(2):105–9.
29. Mahajan R, Koley S. Association of HbA1c with Lipid profiles in patients with type 2 diabetes mellitus. *Int J Biomed Res*. 2016;7(3):139–43.
30. Adninta L, Samsuria I, Limijadi EKS. Correlation between HbA1c and Triglyceride Level with Coronary Stenosis Degree in Type 2 Diabetes Mellitus with Coronary Heart Disease. *J Med Sci*. 2022;10(B):944–8.
31. Naqvi S, Naveed S, Ali Z, Ahmad SM, Khan RA, Raj H, et al. Correlation between Glycated Hemoglobin and Triglyceride Level in Type 2 Diabetes Mellitus. *Cureus*. 2017;9(6):e1347.
32. Gupta G, Aquiqe M, Giri R, Verma S. Correlation between HbA1c level and LDL cholesterol level in ischemic stroke patients. *Int J Adv Med*. 2020;7:741–4.
33. Stratton IM, Adler A. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258):405–12.

Author biography

Aliya Fatima, Postgraduate

R. D. Malathi, Associate Professor

Mohd Iqbal Ahmed, Associate Professor

Cite this article: Fatima A, Malathi RD, Ahmed MI. Evaluation of Dyslipidemia with HbA1c levels in Diabetes Mellitus. *Int J Clin Biochem Res* 2022;9(4):306-310.