

A Comparative Study of Lipid Profile & HbA1c in Type 2 Diabetes Mellitus Patients in a tertiary care hospital in Indore, Madhya Pradesh
Mohammad Imran¹, Shreya Nigoskar^{2*}, Shilpa Mittal³, Shubham Girdhar⁴

1. Mohammad Imran, PhD Scholar, Department of Biochemistry, Index Medical College, Hospital & Research Centre, Malwanchal University, Indore (M.P)
2. Dr. Shreya Nigoskar, Professor & Head, Department of Biochemistry, Index Medical College, Hospital & Research Centre, Indore (M.P.)
3. Dr. Shilpa Mittal, Professor & Head, Department of Biochemistry, Al-Falah School of Medical Science and Research Centre, Faridabad (Haryana)
4. Dr. Shubham Girdhar, Assistant Professor, Department of Community Medicine, Al-Falah School of Medical Science and Research Centre, Faridabad (Haryana)

Corresponding Author: Dr. Shreya Nigoskar, Professor & Head, Department of Biochemistry, Index Medical College, Hospital & Research Centre, Malwanchal University, Indore (M.P)

ABSTRACT

Introduction: Diabetes mellitus is characterized by chronic hyperglycaemia with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Dyslipidaemia in diabetes commonly manifests as raised low-density lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C) levels or elevated triglyceride (TG) levels. Many studies have proposed HbA1c to be used as a biomarker of both glycaemic control and dyslipidaemia in type 2 diabetes mellitus. Study aimed to observe the lipid profile in type 2 diabetes mellitus patients and to find out the correlation between glycated haemoglobin (HbA1c), FBS and lipid profile in type 2 diabetes mellitus patients.

Material and methods: This is a case control study conducted at Index Medical College, Indore, M.P, after taking ethical clearance from the college ethical committee. 150 patients of type 2 diabetes mellitus and 150 healthy controls were taken after obtaining written and informed consent from them. HbA1c, Fbs and Lipid profile were done in cases and controls using appropriate tests. The data was analysed with SPSS. The mean, SD, independent t test and correlation (Pearson 's) test were used to interpret the results.

Results: There was highly significant difference in mean HDL in diabetic patients (38.83 ± 14.98) and controls (51.62 ± 13.20)

Keywords: Lipid Profile, Type 2 Diabetes, Mellitus Patients, HbA1c

Introduction:

Diabetes mellitus is characterized by chronic hyperglycaemia with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.[1] The global figure of people suffering from diabetes mellitus is estimated to rise from current estimate of 415 million to 642 million by 2040. The number of people with type 2 diabetes mellitus is increasing in every country and 75% of people with diabetes mellitus are living in developing countries [2] Prediabetes is also associated with central obesity, dyslipidaemia, and hypertension.[3] According to an ICMR-INDIAB study, prediabetes was 10.3%.[4] Owing to the diagnostic reliance of patients on blood glucose tests, hyperglycaemia is an evident characteristic of diabetes.[5] as the chronic hyperglycaemia is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels due to cardiovascular disease (CVD). Cardiovascular morbidity and mortality is high in the majority of patients with diabetes, in particular with Type 2 diabetes mellitus (T2DM), who are at a 2- to 4- fold higher risk of cardiovascular mortality compared with non-diabetic subjects [16]. However, plenty of the populations could also bear unnoticed hyperlipidaemia, marked by higher triglycerides (TG) levels, along with low density lipoprotein cholesterol (LDL-C) against lower high-density lipoprotein cholesterol (HDL-C). [6] Dyslipidaemia is often coupled with diabetes, and is really the primary cause for atherosclerosis. It is interpreted as a lipid triad, which involves the survival of small but dense, sdLDL, lower HDL, and higher TG. [7-8] as well as increased free fatty acids, increased small dense LDL (sdLDL), which greatly increases their risk for CVD via the process of atherosclerosis. Although hyperglycaemia was associated with atherosclerotic lesion initiation, addition of increasing amounts of cholesterol led to dyslipidaemia, which was the major factor in atherosclerosis progression, independent of hyperglycaemia [17].

Worsening of glycaemic control deteriorates lipid and lipoprotein abnormalities as a growing body of evidence suggests that dyslipidaemia is secondary to insulin resistance or factors closely related to insulin resistance, such as adiposity [18].The combination of hyperglycaemia and dyslipidaemia produces an enhanced atherogenic environment within the circulation which accelerate the progression to atherosclerosis [19] Glycated haemoglobin (HbA1c) is a routinely used marker for long-term glycaemic control. Apart from functioning as an indicator for the mean blood glucose level, HbA1c also predicts the risk

for the development of diabetic complications in diabetes patients.[9] It is a form of haemoglobin that is chemically linked to a sugar by the process called glycation and reflects the weighted mean plasma glucose concentration during the preceding 2-3 months. It is relatively insensitive to short-term lifestyle changes. It is used as a tool for monitoring glycaemic control and quality of care in patients with diabetes [20]. There is an established log-linear correlation between HbA1c and microvascular complications in diabetic individuals [21], but the relationship between HbA1c and macrovascular disease is unclear. Apart from classical risk factors like dyslipidaemia, elevated HbA1c has now been regarded as an independent risk factor for CVD in subjects with or without diabetes [22],

MATERIAL AND METHODS

This study was a case control study carried out in department of Biochemistry, Index Medical College and Hospital in which the patients were selected as per the inclusion and exclusion criteria. 150 patients of Type 2 diabetes mellitus admitted in Department of Medicine, Index medical collage & hospital, Indore and 150 healthy controls were assessed after taking ethical clearance from the college ethical committee. Written and informed consent was also taken.

Inclusion criteria

1. Subjects aged 30-70 years.
2. Diabetic patients diagnosed on the basis of WHO criteria.
3. Subjects ready to give written consent.

Exclusion criteria

1. Type 2 diabetic patients with a history of cerebrovascular event or myocardial infarction.
2. Type 2 diabetic patients with viral disorders.
3. Type 2 diabetic patients with cancer

Table No.1: Association of FBS, HbA1C& Lipid profile level in case and control

Parameters	Case	Control	P value
Fasting Blood Glucose (mg/dl)	187.89±57.70	91.98±9.94	<0.001
(HbA1c) (%)	9.08±2.12	4.91±00.21	<0.001
Total cholesterol	196.47±57.16	158.70±48.03	<0.001

(mg/dl)			
Triacylglycerol (mg/dl)	199.07±105.72	122.47±41.89	<0.001
HDL cholesterol (mg/dl)	38.83±14.98	51.62±13.20	<0.001
LDL cholesterol (mg/dl)	111.62±39.88	99.05±26.65	<0.001
VLDL cholesterol (mg/dl)	46.23±20.75	33.06±17.09	<0.001

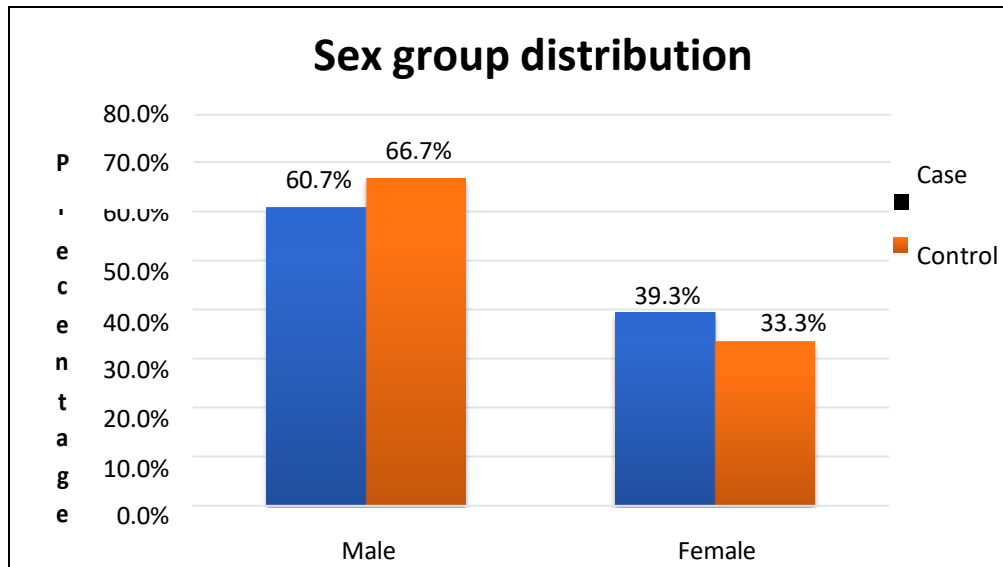
Table 2: Correlation of HbA1c, FBS & PP with Lipid profile

Lipid profile	Pearson's Correlation Coefficient	Fasting blood sugar	Post prandial blood sugar	HbA1c Level
Total cholesterol	r value	0.329**	0.292**	0.324**
	p value	<0.001	<0.001	<0.001
Triacylglycerol	r value	0.417**	0.441**	0.367**
	p value	<0.001	<0.001	<0.001
HDL cholesterol	r value	-0.376**	-0.387**	-0.396**
	p value	<0.001	<0.001	<0.001
LDL cholesterol	r value	0.152**	0.113*	0.152
	p value	0.039	0.050	0.008
VLDL cholesterol	r value	0.342**	0.358**	0.284**
	p value	<0.001	<0.001	<0.001
**. Correlation is significant at the 0.01 level (2-tailed).				
*. Correlation is significant at the 0.05 level (2-tailed).				

In above table represent the Pearson Correlation (Bivariate analysis) of lipid profile, with the diabetes profile and observed a significantly positive association of total cholesterol, triacylglycerol, LDL cholesterol and VLDL cholesterol with FBS, PPBS and HbA1c; while in HDL cholesterol was significant negatively associated FBS, PPBS and HbA1c.

Table No. 3: Sex group distribution

Sex	Group		P value
	Case (n=150)	Control (n=150)	
Male	91 (60.7%)	100 (66.7%)	0.280
Female	59 (39.3%)	50 (33.3%)	

Figure 1: Sex group distribution

In case groups, 60.7% male and rest were female and in control groups 66.7% were male and 33.3% were female patients. By using the chi square test, we find insignificant distribution in both groups ($P>0.05$).

Table No. 4: Age group distribution

Age (Years)	Group		P value
	Case (n=150)	Control (n=150)	
≤40	29 (19.2%)	38 (25.3%)	<0.001
41 – 50	32 (21.3%)	42 (28.0%)	
51 – 60	54 (36.0%)	60 (40.0%)	
>60	35 (23.3%)	10 (6.7%)	

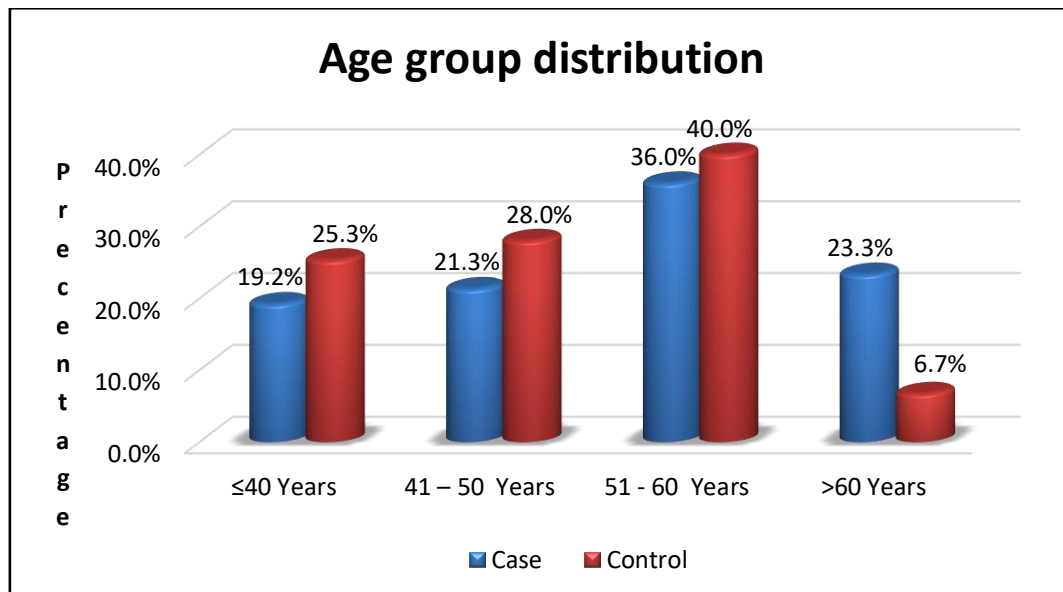
Table No.5: Anthropometric variables

	Group		P value
	Case (n=150)	Control (n=150)	
Age	53.30±11.15	50.07±9.34	0.007
Weight	74.94±10.68	70.75±10.40	<0.001

Height	163.07±7.42	163.73±6.81	0.418
BMI	28.25±4.18	26.46±4.14	<0.001

Above table shows the anthropometric distribution of the studied patients; we observed the statistically significant higher age, weight and BMI in case group in compare to control group ($P>0.05$). But height was almost equal in both groups.

Figure 2: Age group distribution



Majority of the studied cases were in age group of 51 – 60 years. We found that the statistically significant higher older age population in case group distribution in comparison to control group ($P>0.05$).

STATISTICAL ANALYSIS

- Statistical analysis was conducted by using SPSS version
- Unpaired t test was used to calculate significance (p value) in between the groups.
- $p < 0.05$ was considered statistically significant.
- Correlation was determined by using Karl's Pearson's correlation coefficient.

RESULTS

In the present study, 300 subjects were studied of which 150 Type II Diabetes cases, whereas 150 healthy subjects as controls. The mean age of type 2 diabetic subjects had higher 53.30 ± 11.15 years and in 50.07 ± 9.34 years for healthy controls. Similarly, the mean body mass index (BMI) of the Type II

diabetes subjects was higher 28.25 ± 4.18 as compared to 26.46 ± 4.14 healthy controls [table N0.5]

There was highly significant difference in mean HDL in diabetic and control patients ($p < 0.0001$) [table No1]

The mean cholesterol level was slightly higher in Diabetics than normal participants ($P < 0.001$). When valued against controls, the mean triglyceride level of diabetes patients was substantially higher ($P < 0.001$). The average score of LDL-C in diabetics was distinctly higher ($P < 0.001$) than the mean value of controls.

The mean level of very low-density lipoprotein (VLDL) cholesterol in diabetics was clearly elevated ($P < 0.001$). There was significantly positive association of total cholesterol, triacylglycerol, LDL cholesterol and VLDL cholesterol with FBS, PPBS and HbA1c; while in HDL cholesterol was significant negatively associated FBS, PPBS and HbA1c. [table No1]

DISCUSSION

This study also demonstrates the typical diabetic dyslipidaemia which is characterized by low HDL, high triglyceride (Table 1). Various national and international epidemiological studies on lipid profile have also shown this pattern of dyslipidaemia. [10,11]

Liu Y et al conducted a prospective study on western Indian population that comprised of 430 type 2 diabetes mellitus patients and 501 non diabetic control subjects. They found significant correlation of HbA1c with TC and LDL. [12]

A study carried out on 128 type 2 diabetes mellitus patients in Sichuan, China. found significant correlation of HbA1c with LDL. [13]

The mean age of subjects with Type II diabetes was 52.77 ± 12.17 and for controls were 49.73 ± 9.96 This was in accordance with previous research of Sabzwari et al. [14] This present research shows that the BMI was observed to be elevated in Type II diabetes as compared to non-diabetic subjects which was statistically significant. These findings were in accordance to the study of Shahid and Mahboob.[15]

There was a high proportion of dyslipidaemia in this study evidenced by hypercholesterolaemia-TC (60%), LDL-C (65.4%), hypertriglyceridaemia (14.5%), and low HDL-C (41.7%). This is consistent with the findings by Yan et al. [23]

It is suggested that insulin resistance has a central role in the development of diabetic dyslipidemia. One of the causes is increased free fatty acid release from

insulin resistant fat cells. If the glycogen stores are adequate, these free fatty acids promote TG production which further stimulates apolipoprotein B (apo-B) and Very Low-Density Lipoprotein (VLDL) [24].

In this study, the correlation of HbA1c and lipid profile in T2DM was evaluated, and it was discovered that there was a positive relationship between HbA1c and TC, TG and LDL-C, as well as with the TC/HDL-C and LDL-C/HDL-C, which were all statistically significant ($p < 0.05$). Conversely, there was a negative relationship with HDL-C, and it was also statistically significant ($p < 0.05$). This was similarly reported by Hussain et al. who observed that there was a significant positive correlation between HbA1c, TC, TG, LDL-C and LDL-C/HDL-C ratio [25]

Their correlation between HbA1c and HDL-C was negative and was statistically non-significant. A study in India reported similar findings of direct significant correlation between HbA1c and TC, TG, LDL-C, TC/HDL-C, LDL-C/HDL-C and there was inverse correlation between HbA1c and HDL [26], while another study reported that HbA1c levels had a significant direct relationship with TC, TG and LDL-C but not with HDL-C [27]

CONCLUSION

Diabetic dyslipidaemia or atherogenic dyslipidaemia is characterized by low HDL, high TG and high small dense LDL. Early screening of diabetic patients for dyslipidaemia and early intervention is required to minimize the risk of future cardiovascular mortality.

In our study no significant correlation was observed between HbA1c, FBS and HDL.

and may suggest the importance of glycaemic control as well as managing dyslipidaemia, in a bid to further reduce the risk for cardiovascular disease in patients with T2DM. It is being proposed that HbA1c can be used as an important marker to predict dyslipidaemia in patients with T2DM in addition to glycaemic control, and the results of this study support this.

Reference

1. Bennett HP, Knowler WC, Definition, Classification of Diabetes Mellitus and Glucose Homeostasis. In CR Kahn, GC Weir, GL King, AC Moses, RJ Smith and AM Jacobson editors. Joslin's Diabetes Mellitus, Philadelphia: LWW; 200,331.
2. Powers AC, Diabetes Mellitus: Complications. In DL Kasper, AS Fauci, DL Longo, SL Hauser, JL Jameson and J Loscalzo editors. Harrison's

- Principles of Internal Medicine. New York: McGraw-Hill Education; 2015. p.2399.
3. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care: American Diabetes Association; 2018. p. S13-27
 4. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 15 states of India: Results from the ICMR-INDIAB population-based cross-sectional study. *Lancet Diabetes Endocrinol* 2017;5:585-96
 5. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in non-diabetic subjects with or without prior myocardial infarction. *N Engl J Med* 1998;339:229-34
 6. Rader DJ. Effects of insulin resistance, dyslipidemia and intra-abdominal adiposity on the development of cardiovascular disease and diabetes mellitus. *Am J Med* 2007;120:s12-8
 7. Grundy SM. Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. *Am J Cardiol* 1998;81:18B-25B.
 8. Ginsberg HN, Zhang YL, Hernandez-Ono A. Metabolic syndrome: Focus on dyslipidemia. *Obesity* 2006;14:41-9.
 9. Selvin E. Meta-Analysis: Glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Annals of Internal Medicine*. 2004;141:421.
 10. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R et al. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: phase I results of the Indian Council of Medical Research-India diabetes
 11. Witztum JL, Steinberg D. Role of oxidized low density lipoprotein in atherogenesis. *J Clin Invest*. 1991;88:1785– 92
 12. an Z, Liu Y, Huang H. Association of glycosylated hemoglobin level with lipid ratio and individual lipids in type 2 diabetic patients. *Asian Pacific Journal of Tropical Medicine*. 2012;5:469-471
 13. Abd Elkarim A. Abdrabo et al. Role of glycemic control on lipids profile in diabetic sudanese patients. *Journal of Science*. 2016;6:208-212.
 14. Sabzwari M.J, Ahmad M, Majeed M.T, Riaz M, Umair M. Serum sialic acid concentration and type 2 diabetes mellitus. *Professional Med J* 2006;13:508-10

15. Shahid MS, Mahboob T. Clinical correclation between frequent risk factors of diabetic nephropathy and serum sialic acid. *Int J Diabetes metab* 2006;14:138-44.
16. Hernández C, Candell-Riera J, Ciudin A, Francisco G, Agudé-Bruix S, Simo R. Prevalence and risk factors accounting for true silent myocardial ischemia: a pilot case-control study comparing type 2 diabetic with non-diabetic control subjects. *Cardiovascular Diabetology*. 2011;10: 9-16. Google Scholar
17. Renard CB, Kramer F, Johansson F, Lamharzi N, Tannock LR, von Herrath MG et al. Diabetes and diabetes-associated lipid abnormalities have distinct effects on initiation and progression of atherosclerotic lesions. *J Clin Invest*. 2004;114(5): 659-668. PubMed| Google Scholar
18. Selvin E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. *N Engl J Med*. 2010 Mar 4;362(9): 800-11. PubMed| Google Scholar
19. Regmi P, Gyawali P, Shrestha R, Sigdel M, Mehta KD, Majhi S. Pattern of dyslipidemia in type-2 diabetic subjects in Eastern Nepal. *Journal for Nepal Association for Medical Laboratory Sciences*. 2009;10(1): 11-13. Google Scholar
20. Wright LA, Hirsch I. Metrics beyond hemoglobin A1C in Diabetes management: time in range, hypoglycemia, and other parameters. *Diabetes Technology and Therapeutics*. 2017;19(S2): S16-S26. PubMed| Google Scholar
21. Pettitt DJ, Knowler WC, Lisse JR, Bennett PH. Development of retinopathy and proteinuria in relation to plasma-glucose concentrations in Pima Indians. *Lancet*. 1980 Nov 15;2(8203): 1050-2. PubMed| Google Scholar
22. Ikeda F, Doi Y, Ninomiya T, Hirakawa Y, Mukai N, Hata J et al. Haemoglobin A1c even within non diabetic level is a predictor of cardiovascular disease in a general Japanese population: the hisayama study. *Cardiovasc Diabetol*. 2013 Nov 7;12: 164. PubMed| Google Scholar
23. Yan Z, Liu Y, Huang H. Association of glycosylated hemoglobin level with lipid ratio and individual lipids in type 2 diabetic patients. *Asian Pac J Trop Med*. 2012 Jun;5(6): 469-71. PubMed| Google Scholar

24. Sears B, Perry M. The role of fatty acids in insulin resistance. *Lipids Health Dis.* 2015 Sep 29;14: 121. PubMed| Google Scholar
25. Hussain A, Ali I, Ijaz M, Rahim A. Correlation between hemoglobin A1c and serum lipid profile in Afghani patients with type 2 diabetes: Haemoglobin A1c prognosticates dyslipidemia. *Therapeutic Advances in Endocrinology and Metabolism.* 2017;8(4): 51-57. PubMed| Google Scholar
26. Bhattacharjee P, Das P, Nath BK, Basumatary A, Das D. HbA1C and its correlation with lipid profile in acute myocardial infarction. *International Journal of Contemporary Medical Research.* 2018;5(4): D13-D16. Google Scholar
27. Reddy SA, Meera S, William E, Kumar JS. Correlation between glycemic control and lipid profile in type 2 diabetic patients: HbA1c as an indicator of dyslipidemia. *Asian Journal of Pharmaceutical and Clinical Research.* 2014;7(2): 153-155. Google Scholar